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THE USE OF RESERPINE, CHLORPROMAZINE AND ALLIED DRUGS IN MEDICINE AND PSYCHIATRY.[1]

By DAVID R. MORGAN,
Sydney.

THIS evening Dr. Hilliard and I will describe some of the new drugs which are now being used in medicine and psychiatry in Australia and overseas and which, in the Mental Hospital at Parramatta, have, during the past eighteen months, given most encouraging results in the treatment of the mentally ill.

It is proposed to describe the drugs and their dosage, and with each drug to draw attention to the side-effects which have been observed following our experience; to give a brief outline of what may be expected from the exhibition of each drug; and then to inform you of the actual results of treatment which have been achieved at the Mental Hospital, Parramatta.

The drugs which have been used in the hospital can be grouped in two main categories—namely, "ataraxics" and "anti-depressants" or psychoanaleptics. The term "ataraxic" was first used by Howard D. Fabing (1955) to describe those drugs which produce a freedom from confusion. This is a convenient term, as it describes an overall feature common to all the drugs in this group, and this feature is more noteworthy than the tranquillizing effect which many authors have mentioned in the past. The "ataraxics" are chlorpromazine, reserpine, "Pacatal" and "Frenquel", whilst the psychoanaleptics or antidepressants are "Ritalin" and "Meratran".

CHLORPROMAZINE AND RESERPINE.

As chlorpromazine was the first of these drugs to be tried in our hospital, in the middle of 1954, by Dr. J. L. Evans, it is convenient to consider this drug and reserpine together, as the bulk of our experience has been with chlorpromazine and reserpine. It was only toward the end of 1955 that the other drugs, "Pacatal", "Ritalin", "Meratran" and "Frenquel" became available to us; so that, of course, the experience gained in their use is not so extensive, but it is, nevertheless, very interesting.

Chlorpromazine hydrochloride ("Largactil", "Thorazine" or "Megaphen") is a phenothiazine derivative originally discovered in the Rhône-Poulenc-Specia Laboratories by French workers who had been doing research into the "syndrome of irritation" or "phenomena of Rielly" and were looking for a phenothiazine derivative which had central depressant action with a minimum of peripheral antihistamine-like action. The basic pharmacology of the drug was first described by Courvosier *et alii* in 1953, and

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 26, 1956.

it is postulated that chlorpromazine exerts its central influence through the brain-stem reticular formation (Hopkin, 1955).

Chlorpromazine is closely related chemically to promethazine hydrochloride ("Phenergan"), ethopropazine hydrochloride ("Lysivane") and diethazine hydrochloride ("Diparcol"), all of which are phenothiazine derivatives but have very different pharmacological properties. As a result of the discovery of chlorpromazine, much research is being carried out overseas into other modifications of the phenothiazine nucleus which will modify mental behaviour; one example is N-methylpiperidyl-3-methylphenothiazine ("Pacatal"), which will be mentioned again later.

Next we come to reserpine, and it is astonishing that two chemical substances, so wholly different in origin yet with so many features in common, should have entered the therapeutic field almost together.

Reserpine is an alkaloid derivative of the Indian snake root plant *Rauwolfia serpentina*. These Rauwolfia plants are numerous, and 30 to 40 different species have been discovered. They are named after a German botanist, Leonard Rauwolf, whose investigations of these plants were published in 1582. Dr. S. K. Smith (1955) mentions that Dr. Nathan Hodges found snake root the most effective drug employed in combating the plague in London in 1665, and that in 1670 John Quincy described a property of serpentar (snake root) as follows: "Its warmth occasions it to be useful in nervous disorders"—an observation which has since received overwhelming confirmation.

In the autumn of 1953 Swiss workers isolated reserpine from among 14 different pharmacologically active alkaloids found in *Rauwolfia serpentina*, and among these is the hallucinogen yohimbine, which, as will be seen, has a vaguely similar formula to reserpine.

It has been shown that reserpine is the alkaloid primarily responsible for the action of the whole root of *Rauwolfia serpentina* (Bein, 1953), and that rescinnamine has a similar but weaker action. Another reserpine-like alkaloid, deserpidine (desmethoxyreserpine), obtained from *Rauwolfia canescens*, has been discovered to have a pharmacological action within the range of reserpine. Apart from these alkaloids it seems that no useful purpose can be served by treating mental illness with partial fractionations of Rauwolfia when the alkaloid primarily responsible for its neuro-pharmacological action is readily available, chemically pure and uniformly standardized, namely reserpine.

The Dosage of Reserpine and Chlorpromazine.

The dosage of reserpine and chlorpromazine in our hospital has been modified both by our own experience and by that of overseas investigators; and now a standard pattern of dosage has been adopted for all wards throughout the hospital. The object is to achieve the maximum therapeutic result as rapidly as possible and also to lay down a uniform procedure that can be readily followed by the nursing staff when they are transferred from one ward to another.

The highest dosage of reserpine given to any one patient has been 32 milligrammes per day, although in America 60 milligrammes per day have been given.

Reserpine is issued to the wards in tablets of one milligramme and in ampoules of one milligramme (Ciba). On the first day the patient receives four milligrammes of reserpine (that is, two tablets each of one milligramme twice in the day), on the second day eight milligrammes (that is, four tablets twice in the day) and on the third day 12 milligrammes (that is, six tablets twice in the day). This third-day dosage is maintained until a clinical response is obtained; and by this is implied not merely drowsiness and slowness of movement, but also evidence that the patient is more realistically in contact with the environment and evidence of lessening of the patient's symptoms. When this stage is reached, or in any case at the end of three weeks, the dosage is then reduced by not more than four milligrammes a day to a maintenance dosage, which in the vast majority of patients has been found to lie between two and four milligrammes per day.

Chlorpromazine is administered according to a similar schedule; but in this case "100 milligrammes" should be substituted for the "one milligramme" given above.

The largest dose of chlorpromazine given to any one patient has been 1800 milligrammes per day, although Kinross-Wright, in America, has given up to 4000 milligrammes per day.

Chlorpromazine ("Largactil") is supplied in 100 milligramme tablets and 50 milligramme ampoules (May and Baker). On the first day the patient receives an oral dose of 400 milligrammes, on the second day 800 milligrammes, and on the third day 1200 milligrammes (that is, six tablets twice a day), this dose being continued until a clinical response is obtained; then the dosage is reduced (in a similar manner to that outlined above) to a maintenance dose, which is generally of the nature of 200 to 400 milligrammes per day.

Of course, with both reserpine and chlorpromazine, it may be that on the second day the clinical improvement may be such that there are no grounds for further increasing the dose beyond four tablets morning and evening. Each patient's progress is therefore discussed with the sister in charge of the ward, and future treatment is determined in the light of this clinical evaluation.

When chlorpromazine and reserpine are used concurrently, it is usual to employ half the standard dosage of each. Thus, on the third day such a patient would receive six milligrammes of reserpine and 600 milligrammes of chlorpromazine—still a total of 12 tablets (that is, three tablets of each drug morning and evening). There seems to be no advantage in using larger doses than those outlined above, as beyond this range there is a greater possibility of producing a syndrome which resembles Parkinsonism and which can be disturbing to the patient, even when partially controlled with ethopropazine hydrochloride ("Lysivane"). Some authors have suggested that it is necessary to produce a clinical response of this nature in order to achieve a maximum therapeutic result; but this has not been found necessary in our hospital.

In the administrations of both reserpine and chlorpromazine it has been found that the intramuscular route is the most efficacious, but with the large numbers of patients and the relative inexperience of many of our nursing staff, the intramuscular route was reserved for those patients who were uncooperative and who refused to take tablets.

Usually chlorpromazine is given undiluted by the intramuscular route, but in elderly, thin, debilitated patients this method of administration may lead to the formation of hard, indurated swellings in the muscle; this, in such patients, may predispose to bed-sore formation. It has been found that this difficulty can easily be overcome by giving the chlorpromazine with "Rondase", which promotes rapid absorption.

Side Effects of Chlorpromazine and Reserpine.

Very many side effects have been observed during the treatment of our patients, both with chlorpromazine and with reserpine, but none of them have proved fatal, and all can be either controlled or eliminated. It is necessary to adopt a scheme of classification of these side effects which can be readily followed and which conforms with overseas experience. The headings suggested by Kinross-Wright (1955) will be used: Group 1: Local irritation of mucous membranes. Group 2: Parasympathetic effects and nasal congestion. Group 3: Disturbances of central regulating mechanisms. Group 4: Sensitivity reactions. Group 5: Parkinsonian-like side effects.

It should be noted that the side effects of chlorpromazine are diverse and can be considered under all five headings, whilst those of reserpine are generally confined to groups 2, 3 and 5.

Group 1.

Side effects in group 1 are relatively unimportant, but several patients have complained of sore mouths and occasionally of diarrhœa. In one case treatment with chlorpromazine was suspended for two days when the patient's tongue became tender and somewhat swollen.

Group 2.

The side effects in group 2 occur with both drugs. By far the commonest of them is nasal stuffiness and congestion, which some patients have found very trying over a period of time, but which is relieved by the use of ephedrine saline nasal drops on retiring. Here also are included hypotensive effects and tachycardia, which are commonly observed but which seldom call for cessation of therapy. Other patients have had distressing salivation with partial loss of the swallowing reflex, and this is often associated with other extrapyramidal signs. This ceases to be a problem as the patients reach a maintenance dosage. The miosis, constipation and bradycardia mentioned by some authors have not been encountered in our series of cases.

Group 3.

Side effects referable to disturbances of central regulating mechanisms have been greater with chlorpromazine than with reserpine. Some patients have complained of a subjective sensation of feeling cold and of shivering, even when sitting in the sun. Others, during the first few days of treatment, have rises in temperature not associated with infection; and yet others have developed œdema of the face—especially of the eyelids and lips. Œdema of the four extremities has also been encountered. This œdema is definitely not nephritic in origin, and it is considered to be a posterior pituitary-hypothalamic effect. It disappeared in a few days when the dosage was temporarily decreased and did not recur if the dosage was raised subsequently. Very noticeable was an increase in appetite in many patients with consequent gain in weight. Their weight tended to decrease to some extent as treatment progressed; and, in general, it could be said that the patients appeared relaxed, happy and contented people who enjoyed their meals.

Two female patients receiving chlorpromazine have had a small flow of fluid from their breasts, not associated with pregnancy, which lasted two to three weeks and gradually disappeared. None of our female patients complained of any change in their menstrual pattern.

Somnolence and lack of drive were common to most patients in the early stages of treatment; but as they became stabilized on maintenance dosage their affect and drive became appropriate and normal. This drowsiness was usually directly related to dosage.

When patients complained unduly of being distressed by a feeling of lethargy, it was found that this could be relieved successfully by administering one to two milligrammes of pipradrol ("Meratran"—Merrell) three times a day, 10 to 20 milligrammes of phenidylate ("Ritalin"—Ciba) twice a day, or five to ten milligrammes of dexamphetamine once or twice daily.

Three patients who had not previously had epileptic seizures had one or two fits during the early stages of treatment. These fits, for which antiepileptic drugs were given, were considered to be due to cerebral irritation having the same basis as the œdema mentioned above. Dosage was not reduced; and they have had no further fits in the nine months since their antiepileptic drugs were withdrawn.

Group 4.

Sensitivity reactions, included in this group, were found exclusively in patients receiving chlorpromazine, and they occurred in approximately 8% to 10% of the patients. A variety of skin rashes have been seen, including discrete punctate erythemas, morbilliform eruptions, maculo-papular rashes such as are seen in drug idiosyncrasies, and one case of generalized erythema somewhat resembling scarlet fever. Several patients developed an exfoliative eczematoid reaction resembling *seborrhœa sicca* which cleared in two to three weeks. Erythema of the face, hands, lower parts of the legs and feet was observed early in this treatment; but this was obviously a photosensitivity effect caused by sunlight. It cleared rapidly when patients were kept indoors in the shade.

In all the above cases the patients were helped by being given antihistamines.

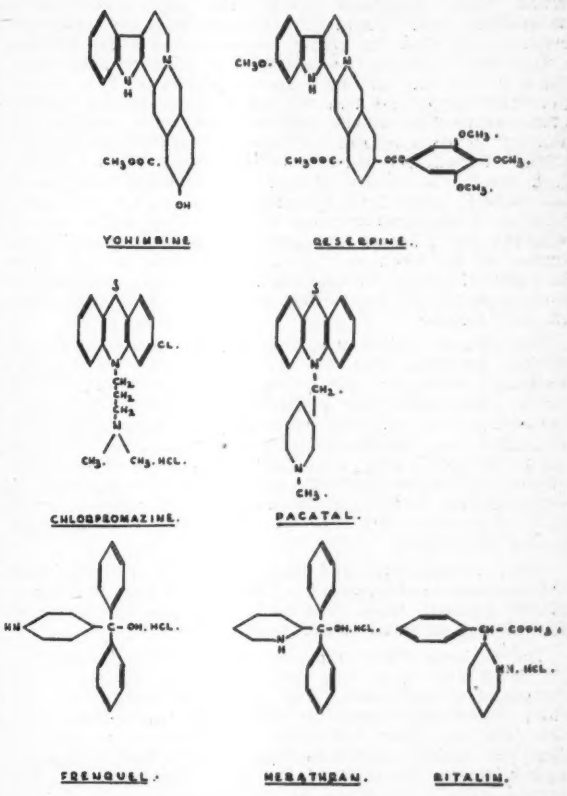

FIGURE I.
Chemical structure of drugs discussed.

Pollack (1955) and Denber (1955) mention skin rashes occurring in staff administering chlorpromazine, and it is of interest that seven members of our nursing staff (three males and four females) have developed typical contact dermatitis of the hands and face from giving injections of chlorpromazine to the patients. Our nurses are now instructed to use gloves when giving injections of this drug.

Only one patient has developed jaundice among nearly 400 who have been treated with chlorpromazine.

This patient, aged seventy-eight years, when admitted to hospital was agitated, restless, confused, demented and incoherent. She was given 25 milligrammes of chlorpromazine three times a day because of her extremely frail condition, and a little over a fortnight later she developed jaundice. This jaundice was shown to be obstructive in type and was accompanied by relative eosinophilia. Chlorpromazine therapy was temporarily suspended, and she was treated with antihistamines. When the jaundice subsided chlorpromazine therapy was recommenced with 100 milligrammes twice daily, and the jaundice did not recur.

Usually, chlorpromazine jaundice develops during the first two to three weeks of therapy, and then more frequently in patients receiving a relatively small dosage. The consensus of opinion seems to be that it is a sensi-

tivity reaction; and this is substantiated by the fact that there is often a relative eosinophilia (Lomas, Boardman and Markowe, 1955). The question of jaundice in patients is discussed by Cohen and Archer (1955) and Isaacs, MacArthur and Taylor (1955).

Group 5.

Of our patients, 10% to 12% developed side effects which are best described as being extrapyramidal in origin. When these symptoms were first encountered, they occasioned some disquiet; but now that they can be readily controlled, by giving ethopropazine hydrochloride ("Lysivane"), one to two tablets of 50 milligrammes three times a day, they are no longer a problem. These extrapyramidal symptoms run the whole range from a mildly blank expression on the patient's face with slowness of smiling to an appearance typical of Parkinsonism—head slightly bowed, eyes staring straight ahead, saliva running from the mouth because of lack of spontaneous swallowing movements, arms held slightly flexed beside the body, with no swinging movements, as the patient walks with a shuffling gait. Some patients developed a rhythmical tremor of the hand and wrist, very similar to that seen in cases of senile Parkinsonism, but to our examination these patients did not exhibit the rigidity frequently seen in that disease.

One patient receiving chlorpromazine developed a surprising reaction. She was at times unable to initiate walking movements—she would stop suddenly, then continue; occasionally she would stop and take a few steps backwards. She was very concerned over this, saying that she could not help it, no matter how hard she tried to walk normally. This was regarded as being a variation of extrapyramidal symptomatology; and with the help of ethopropazine hydrochloride she has been able to walk quite naturally again, although she is still somewhat slow in her movements.

Another interesting and little known side effect of both chlorpromazine and reserpine has occurred in over a dozen of our patients, when on both high dosage and maintenance dosage as small as one tablet twice daily.

The patients state that they feel drowsy and want to sit down and relax, yet they cannot do so. They feel compelled to walk about and move their arms. They do this slowly and naturally; yet if they sit down they complain that they feel tense and cannot relax, and in fact one patient continued to walk and walk until she had blistered the soles of her feet. This symptom has proved difficult to treat, as it was considered wise to avoid barbiturate sedation if possible. It was found that the majority of patients were controlled with "Lysivane", and the remainder obtained relief from promethazine hydrochloride ("Phenergan"), 25 milligrammes twice a day, which has the slight disadvantage that although the patients were able to relax they remained drowsy. This drowsiness could be alleviated by the administration of "Ritalin", but the treatment then became rather cumbersome—treatment to treat the treatment does not seem a very sound procedure if it can be avoided.

It is of interest to note that these extrapyramidal signs developed with greater frequency (18%) in the 60 patients who received combined therapy with chlorpromazine and reserpine than when either drug was used alone, and it is felt that these drugs are synergistic in this respect.

A word of warning should perhaps be issued concerning the giving of opiates to patients receiving chlorpromazine. One patient about to undergo herniorraphy was given "Omnopon" pre-operatively and collapsed in the theatre prior to the administration of the anæsthetic, remaining in a deeply comatose state for four hours, after which he gradually regained consciousness and fortunately suffered no ill effects.

It has also been found that patients who contract an intercurrent infection, such as a cold, and who are receiving chlorpromazine seem to become more ill than would normally be expected. It has been found desirable to reduce dosage in these cases as, in some manner, the drug seems to interfere with the natural defence mechanisms of the body. Should patients develop pneumonia, the chlorpromazine therapy is usually discontinued while their temperature is elevated.

A potential danger—namely, the risk of suicide, associated with the administration of reserpine in general practice—has been already mentioned by Swanton (1955). It has also been noted in our hospital that some patients taking reserpine develop a pathological depression. This state seems to arise most frequently in agitated, depressed hypertensives who go to their own general practitioner for treatment of their hypertension; when this is controlled with reserpine they are calmed and lose their motor restlessness, although they still retain their depression. It is then that they are able to plan what may easily prove to be a successful suicidal attempt. Of course, this is not a problem in a psychiatric hospital, where the patient is under constant supervision, and the depression can be treated either by electroconvulsive therapy or by one of the newer psychoanaleptics such as "Ritalin" or "Meratran".

The question of combining reserpine with electroconvulsive therapy arises. This combination has rarely been used in treating our patients because it was our aim to see how far new drugs could replace former therapies. However, a word of warning is sounded by Foster and Gayle (1955) in a report on a series of 63 patients. They state that one patient died and five others were severely shocked for some hours after electroconvulsive therapy when the patients were receiving reserpine at the same time. These authors suggest that an interval of at least one week should elapse between the cessation of reserpine therapy and the administration of electroconvulsive therapy.

In our hospital it is the custom to give 0·25 gramme of thiopentone with 50 milligrammes of "Brevedil E" when muscle relaxants are used with electroconvulsive therapy. One patient, aged seventy-four years, hypertensive with an intense agitated depression, who was receiving 200 milligrammes of chlorpromazine twice a day and 40 milligrammes of "Ritalin" twice a day, was given electroconvulsive therapy, and she suffered a respiratory collapse and did not recommence normal breathing till six minutes had elapsed. During this time she was given oxygen, artificial respiration and "Coramine". She then made an uneventful recovery. It is thought that in this instance the chlorpromazine potentiated the action of the intravenously administered thiopentone—a complication which could be serious.

An extensive survey of the complications of chlorpromazine therapy has been given by Kinross-Wright (1955). From the experience gained with our patients, however, it is felt that these drugs can be used in quite large doses with perfect safety under hospital conditions when treatment can be adequately supervised. In this connexion, the comments of Denber (1955) are of interest. He pointed out that chlorpromazine had been used in the treatment of more than five million patients, and that the total incidence of the various reactions was very small. One cannot but agree with his comment that the side effects have been stressed out of all proportion, and that this attitude may tend to bring into disrepute a drug which is of undoubted value in the therapeutic armamentarium which the psychiatrist now has against a wide variety of mental illnesses. There are risks; but they are indeed small when compared with the risk taken by a patient who undergoes leucotomy, and it is only right that the side effects sometimes associated with the use of chlorpromazine and reserpine should be kept in proper perspective.

"PACATAL."

The next drug to be described is "Pacatal", another ataraxic, supplies of which were generously provided by William Warner and Company.

"Pacatal" is the trade name of Warner-Lambert International for their brand of N-methylpiperidyl-3-methyl-

phenothiazine. It is, like chlorpromazine, a phenothiazine derivative. Besides its use in psychiatry it is used in anæsthesia and in internal medicine to potentiate the action of certain other drugs. Broadly, "Pacatal" may be said to have approximately the same range of action as chlorpromazine, but with far fewer unpleasant side effects. However, it has side effects of its own, which will be described, and these have restricted its general application to a certain extent. The hydrochloride of "Pacatal" is given by mouth and the acetate by injection.

"Pacatal" is supplied in tablets of 25 milligrammes and in ampoules containing 50 milligrammes in two cubic centimetres. The largest daily dose that has been used with this drug is 600 milligrammes per day given as 200 milligrammes three times a day. This drug has been found to be more rapidly effective when given by injection than by mouth.

The only side effects so far noted with "Pacatal" have been a blurring of vision and an intense dryness of the mouth. These atropine-like side effects, although not so diverse as those of chlorpromazine, have been so distressing to a number of patients that administration of the drug has had to be discontinued on several occasions. Because of this, more recently the drug has been used mainly for those patients who fail to show a favourable response to chlorpromazine; and one male patient who still showed violent, aggressive behaviour to the staff on each occasion on which they approached him, even whilst receiving 1200 milligrammes of chlorpromazine per day, has shown a tremendous improvement since being given "Pacatal". It is felt at present that this drug is not a complete substitute for chlorpromazine, which still remains the drug of choice in spite of its many side effects. However, "Pacatal", with its relatively few side effects, has a very real place in the treatment of tension and aggression associated with delusions, and patients who fail to respond to chlorpromazine should be given the benefit of a therapeutic trial with "Pacatal". This drug has been found to be a valuable adjunct to chlorpromazine therapy, especially in the treatment of obsessional states. Later, Dr. Hilliard will give our results of treatment with this drug, and it is of interest that the drug has also been used at Callan Park by Dr. S. G. Sandes. From our experience it can be used with perfect safety in the treatment of debilitated elderly patients, and it is more readily absorbed by the tissues than chlorpromazine. It can be used in combination with chlorpromazine as well as electroconvulsive therapy; and with two of our patients it has appeared to have a synergistic effect with "Frenquel". However, these impressions are too few to have statistical validity.

"FRENQUEL."

The most recent ataraxic we have used is "Frenquel", but with only two months' clinical experience it would be unwise to be dogmatic with claims for this drug.

"Frenquel" is the trade mark of the William S. Merrell Company for its brand of azacyclonol, and the product is the result of original research by that company, which generously made available to us the "Frenquel" used in this study.

The chemical formula of "Frenquel" is α-(4-piperidyl) benzhydrol hydrochloride, and it is the γ-isomer of "Meratran". It prevents the central stimulation induced in the mouse by cocaine, morphine, amphetamine and "Meratran". It was first studied by Fabing in 1954-1955 and found to have a therapeutic effect against certain dissociation syndromes and later as a blocking agent against the model psychoses induced by L.S.D. 25 and mescaline. Fabing's reports of the therapeutic effect of "Frenquel" on the hallucinations associated with acute schizophrenia, alcoholic hallucinations and senile and arteriosclerotic states made us most anxious to try the drug on our patients, even though he stated that the results obtained within the dosage range used were inconsistent.

After receipt of a personal communication from Dr. Pogge of the William S. Merrell Company, Department of Medical Research, "Frenquel" has been administered in the following manner. "Frenquel" is supplied in 20 milligramme tablets and 100 milligramme ampoules. Patients are given 100 milligrammes intravenously, and eight hours later this dose is repeated. On this first day the patient is also given one 20-milligramme tablet three times a day by mouth, and this oral dosage is then maintained throughout the course of treatment. So far, no side effects

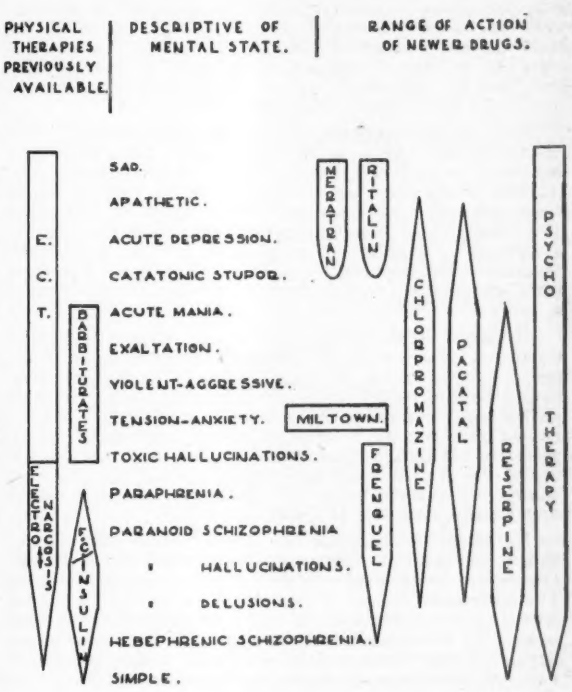

FIGURE II.
Therapeutic range of various types of treatment.

referable to "Frenquel" have been noted in our patients; nor have side effects been noted by overseas observers such as Fabing and Hawkins (1955) in their first 115 cases, when some patients were given up to 400 milligrammes per day for periods of up to six weeks.

This absence of side effects leads to the question of possible overdosage with "Frenquel".

In a communication from the manufacturers the L.D.50 (the lethal dose for half the animals tested) was 177 milligrammes per kilogram for intravenous injection. In an average adult patient an intravenous dosage of 600 milligrammes per day is approximately 10 milligrammes per kilogram; thus it is seen there is a wide margin of safety even when high doses of "Frenquel" are used. It is of interest to note that of the first 358 patients treated in the United States who were suffering from schizophrenia 190 were said to have achieved a favourable response. It is also claimed that the drug is synergistic to chlorpromazine and enhances the effect of electroconvulsive therapy in schizophrenia.

ANTIDEPRESSANTS.

We now come to the "antidepressants" or psychoanaleptics "Ritalin" and "Meratran", both of which have an amphetamine-like central stimulant effect, but without the undesirable side effects of the amphetamines, such as sweating, anorexia and pressor effects which so often preclude the safe use of amphetamines in cases of severe hypertension. Also, patients do not experience tachy-

cardia and do not complain of the subjective sensation of their hearts pounding in their chests, which one patient described to me as feeling like "a cat in a bag".

This absence of side effects has enabled us to use these drugs in depressed hypertensives with most encouraging results.

"Ritalin" and "Meratran" enhance the mood without causing a foolish restless euphoria. Depressed patients become more cheerful and cooperative, are able to wash, feed and clothe themselves and, even when still depressed, show increased motor activity and are able to carry on conversations instead of remaining mute and inaccessible. Only one patient complained of difficulty in sleeping and that only for two nights; apart from this, no side effects have been noted with either drug.

Ciba, Limited, generously supplied the "Ritalin" used in this study, and it is the trade name for their brand of phenyl-(α-piperidyl) methylacetate hydrochloride. Our interest in the drug was first stimulated by reports of its favourable effect on reserpine-induced states of depression (Ferguson, 1955), and our experience has confirmed this observation. "Ritalin" is supplied in tablets of 10 milligrammes, and the dosage used in our hospital has been from one tablet twice a day to two tablets three times a day.

"Meratran" is the trade mark of the William S. Merrell Company, who generously supplied the drug used in the study, for its brand of pipradrol or α-(2-piperidyl)benzhydrol hydrochloride. Pharmacological studies of its effect on laboratory animals were first published in 1953 by Brown and Werner. Since that time numerous investigators in the United States have reported favourably on the use of the drug in depressive states, perhaps the two most interesting reports being by Schut and Himwich (1955) and Fabing, Hawkins and Moulton (1955).

"Meratran" is supplied in tablets of one milligramme and in combination with reserpine as tablets of one milligramme of "Meratran" and 0·25 milligramme of reserpine. The customary dosage of "Meratran" for patients suffering from reactive depressions is one to two tablets three times a day. In this hospital up to eight tablets three times a day have been given, and in the United States narcoleptic patients have been given 100 milligrammes daily for over a year with good results. Thus it appears that the drug has a wide margin of safety, and no side effects have been observed in any of our patients receiving the drug.

These drugs have been of the utmost assistance in treating our depressive patients; both seem to be equally effective, and the combination of "Meratran" and reserpine seems to have a definite place in the treatment of patients suffering from agitated depression. It is most encouraging to note the manner in which patients who have been slow and lethargic when receiving chlorpromazine or reserpine assume a normal mode of behaviour when treated with these antidepressive drugs—and of course reserpine depression is no longer a problem, as mentioned earlier.

It seems from our experience that now "Ritalin" is available and it is hoped that "Meratran" soon will be, these drugs will have a wide field of application in the treatment of the psychoneuroses and in general practice, perhaps much more so than in a mental hospital.

From what has been said it will be seen that we now have drugs which will treat patients with hallucinations, delusions, agitation, tension, aggression and manic states; and whilst there are also drugs which will treat patients with depression, those with this latter illness, when it is acute, still respond best to electroconvulsive therapy. It is true, however, that with "Meratran" and "Ritalin" the number of shock treatments required to alleviate depression is very much fewer than was formerly required. These drugs have liberated the vast majority of patients from the unreasoning fear most have of electroconvulsive therapy. In our hospital no electroconvulsive therapy has been given in the main female division since July, 1955, and in our male admission ward since November, 1955; and at the present in the female admission ward there are only three acutely depressed patients out of 65 who are receiving electroconvulsive therapy. Our attempt to eliminate electroconvulsive therapy completely as the main method of treating psychoses has been almost successful and may well be so in the not far distant future.

The six drugs, chlorpromazine, reserpine, "Pacatal", "Frenquel", "Ritalin" and "Meratran" all have one thing in common—namely, that their site of action is, almost certainly, on the "mesodiencephalic activating system", called for short M.D.A.S., in the mid-brain reticular formation. This portion of the mid-brain is situated just above the superior *corpora quadrigemina* and includes the reticular formation of the brain-stem tegmentum of Moruzzi and Magoun as well as the diffuse thalamic projection system of Jasper.

The manner in which the drugs are presumed to act on the mesodiencephalic activating system (M.D.A.S.) is a fascinating but complex story and has been elicited mainly by electroencephalographic studies carried out by Rinaldi and Himwich at the Thudichum Psychiatric Research Centre of the Galesburg Research Hospital in Illinois.

There are a number of associated concepts linked with the probable site of action of the drugs on the brain-stem reticular formation and the septal nuclei of the hypothalamus, which may yet be integrated into an harmonious whole, to serve as an electro-neuro-pharmacological explanation of what is at present called "functional mental illness". Enumerated, they are as follows:

1. In 1940-1942 Pauline Davis demonstrated that specific electroencephalographic patterns are to be found in cases of schizophrenia.

2. The action of histamines and antihistamines is closely interwoven with the action of adrenaline. Antihistamines and adrenaline are both used in allergic and hypersensitivity reactions.

3. Insulin has a diametrically opposite effect to that of adrenaline, and for many years full coma insulin has been used with success in treating patients suffering from schizophrenia.

4. Electroconvulsive therapy is thought to exert its beneficial effect on the hypothalamic area.

5. Some drugs which are now used to treat mental illness are phenothiazine derivatives closely related to the antihistamine promethazine hydrochloride "Phenergan".

6. Rinaldi and Himwich in 1954 showed the site of action of the anti-Parkinsonism drugs to be in the mid-brain reticular formation.

7. The anti-Parkinsonism drugs "Lysivane" and "Diparcol" are also phenothiazine derivatives, as are chlorpromazine and "Pacatal", the latter having atropine-like side effects; and atropine too can be used to modify the symptoms of Parkinsonism.

8. "Meratran" elicits a pattern of alertness in the electroencephalogram of the M.D.A.S., whilst atropine has the opposite effect.

9. In our hospital reserpine has been used experimentally, and with success, to control the tremor of Parkinsonism and Huntington's chorea (Morgan, 1956).

10. Reserpine has been shown by Rinaldi and Himwich (1955*b*) to exert its influence on the M.D.A.S.

11. It has been considered that the reticular formation is the translating mechanism for the autonomic activity associated with emotion.

12. Strong emotion and tension liberate adrenaline, and Fabing, in his presidential address to the seventh annual meeting of the American Academy of Neurology in 1955, has suggested that the breakdown of adrenaline to adrenochrome, which has been shown by Osmond, Hoffer and Smythies (1954) to be an hallucinogen, may be the cause of hallucinations in schizophrenia.

13. Fabing has also suggested other possible mechanisms for the breakdown of naturally occurring indoles in the body to hallucinogens.

14. Fabing has also shown that the hallucinations produced by the hallucinogens L.S.D. 25 and mescaline can be blocked by "Frenquel".

We have found the interrelation of the above facts most stimulating and intriguing; but how to correlate them into a coherent, unifying concept is beyond us at the present state of our knowledge.

We now have drugs which will modify or remove many of the symptoms of mental illness. This removal of symptoms need not necessarily mean the cure of disease, in the same way as the control of the symptoms of diabetes with insulin or epilepsy with "Phenytoin" does not mean that those diseases are cured. Mental illness is ultimately the development of faulty habit patterns of reaction to environmental stress, and these new drugs, which have been described, enable the patient to establish new behavioural patterns which, with psychotherapy, eventually become stable and healthy ingrained habits.

We believe that psychotherapy is still the basic means of treating mental illness, and that these new drugs modify the symptoms of mental illness to the extent that the patient becomes more receptive to new ideas and can see reality as others see it.

We stand at the threshold of a new era in the treatment of mental illness, in which the symptoms of the illness, rather than the disease itself, will be able to be treated with the same precision as the physician now treats other metabolic diseases.

Dr. Hilliard will now tell you of the actual results of treatment which have been achieved at the Mental Hospital, Parramatta.

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THE USE OF RESERPINE, CHLORPROMAZINE AND ALLIED DRUGS IN MEDICINE AND PSYCHIATRY.[1]

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A RECAPITULATION of the different drug treatments for schizophrenia during the last quarter of a century may be of interest, if only to demonstrate the varying methods of attack.

Twenty-five years ago the treatment *par excellence* of schizophrenics was thyroid feeding; the patient was placed in bed and given thyroid extract in five-grain doses, the dose being increased by five grains every other day until symptoms of hyperthyroidism developed, when the treatment was discontinued. A large number of simple and hebephrenic schizophrenics did recover, while others disappointingly were not in any way improved. This treatment fell into disuse and is now very rarely used. However, interest in the use of thyroid extract might be reawakened by the recent work of Cranswick, who in 1955 carried out tracer iodine studies on thyroid activity and responsiveness in schizophrenia, and after comparing results with those of controls, reached the conclusion that schizophrenics live under such stress as to produce thyroid fatigue.

Other methods of attack on schizophrenia were directed at remedying the known leucopenia existing in the disease, but the exhibition of nucleinate of soda and other drugs either failed to produce a leucocytosis or, if they did so, did not improve the patient's condition.

Maniacal patients were treated with bromides, chloral hydrate, paraldehyde and an ever-widening range of barbiturates, all directed at allaying the boisterousness of the patient and giving him much-needed sleep. Some of the later barbiturates, particularly "Dial" and "Didial", used in conjunction with hydrotherapy, were extremely efficient and saved many a patient from death from exhaustion.

In passing it may be noted that the disease classified by Stoddard and others as acute delirious mania, which he considered the only mental illness immediately dangerous to life, has now practically disappeared, probably owing to the increased facilities for treatment possessed by the general practitioner, who formerly and probably still sees this disease in its incipient stages.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 26, 1956.

The treatment of melancholia other than correction of the physical accompaniments of the disease consisted in the exhibition of tincture of opium in increasing doses until the optimum dosage for the patient was reached. Care was taken that the opium should not increase the constipation present, by combining it with an adequate dosage of an aperient. Occasional good results were obtained by treatment with thyroid extract.

The treatment of confusional states consisted of careful nursing *plus* the exhibition of sedatives or cardiac stimulants, as the case demanded.

Although many of these treatments appear crude and unscientific today, it must be remembered that they resulted in a recovery rate of over 30%.

If we allow for the individual preference of certain psychiatrists, the above treatments persisted until the mid-thirties, when "Cardiazol" was introduced. The theory that epilepsy and schizophrenia occurring at similar ages displayed different symptoms and therefore might be antagonistic diseases led to the search for a fit-producing drug. "Cardiazol" was the answer and was to prove helpful to schizophrenics and more so to the depressed patient. This was the first treatment which required personal administration by the doctor, and therefore its use in acute and chronic mental illness was limited by the number of intravenous injections that any one doctor could give in the course of his duties. For this reason it was rarely used for other than the newly admitted patient; although it was used to a limited extent on chronically affected patients with favourable results.

The main drawback to this otherwise excellent treatment was, firstly, the intense fear that it generated in the patients, many of whom remembered the fear and agitation prior to the onset of the fit, and secondly, the ever-present risk of fracture caused by the violence of the muscular action in the fit. The first factor sometimes deterred patients from continuing with their treatment, particularly in private practice and psychiatric clinics, while the second factor always threatened the completion of a full course of treatment. Elaborate methods were evolved of handling the patient in preparation for the fit. Here for the first time the doctor and the psychiatric nurse were in attendance on the patient at one and the same time.

Since the production of a fit had had such a curative effect in many cases of psychosis, a method less distressing to the patient was sought, and electrically induced convulsions were the result. This treatment has stood the test of time and is still regarded as the standard initial treatment. Modifications of the original operation led to variations in treatment—for example, the introduction of electronarcosis, which some observers have claimed as the only treatment for schizophrenia. This treatment is less time-consuming than "Cardiazol" treatment, but suffers from the limitations of being confined to the number of patients who can be conveniently handled by the doctor and staff in one session.

Concurrent with the last two methods of attack on mental illness we have the use of insulin, which requires the operation of a highly trained doctor and staff, who must remain with the patient for a definite period of time, sometimes hours. These limitations prevent the wide use of such treatment in hospitals, and at present only patients considered suitable and likely to benefit can be so treated.

During this same period other drugs have been tried, some with favourable results in specific cases. These are lithium citrate or carbonate for chronically maniacal patients and sodium iodide given intravenously in the treatment of arteriosclerotic dements.

These treatments, though minor in their application, have yielded favourable results and still have their place in the armamentarium of the psychiatrist.

One striking feature of treatment with "Cardiazol" and electroconvulsive therapy was that the period of residence of the patient in the hospital was reduced appreciably; for example, a melancholic patient, who formerly passed through an illness of three to six months, might be restored to health in six weeks.

However, many patients have proved resistant to one or more of the treatments previously mentioned, and it is to this group that treatment with chlorpromazine and reserpine has been specially directed.

The purpose of this study was to investigate the psychopathological effects of chlorpromazine and reserpine in a group of disturbed female patients who had been in hospital for such a period of time as to be regarded as "chronic". The case material presented in the main is that of patients unrelieved by previous treatment, the illness of some dating back to the late thirties, and representing a number whose response to "Cardiazol" had been unsatisfactory.

It will be recollected that the introduction of "Cardiazol" to chronic wards of mental hospitals had excellent effects resulting in a recovery rate of 50% from these wards. The treatment was adequately summarized by Barry and led him to the hope that continuation of such treatment might ultimately "empty the refractory ward of mental hospitals". This hope was not realized, although the treatment was superseded by the introduction of the more easily administered electroconvulsive therapy. This produced similar results in the chronic wards, where another 50% of patients, many of them chronic depressives, were able to leave hospital. Of the remainder, only a small proportion responded in any way favourably to electroconvulsive therapy — a variable figure in different hospitals, approximately 5% in Parramatta. These patients required biweekly maintenance shock treatments, and cessation of treatment led to a slow but gradual relapse requiring reintroduction of treatment.

Only in a few spectacular cases did patients recover from this group. The remaining patients had been quite uninfluenced by "Cardiazol" or electroconvulsive therapy, and constituted an impulsive turbulent group, frequently in restraint, and spending their time in idleness, violence and destruction.

It is this residue of chronic patients who were the particular objects of investigation in the present study.

It is perhaps significant that the method of choice in each three attacks on the problem of chronic mental illness should be along the same lines. It is the privilege of the writer to have been associated with each of the three. In each case the most disturbed patients were selected by me at the request of the interested medical officer, and the initial results in each case were the same. However, in this investigation the continued enthusiasm of the medical officer, Dr. Morgan, resulted in an extension and an amplification of the treatment, so that all types of mental disease leading to chronicity were ultimately considered.

The case material presented covers the use of chlorpromazine and reserpine on a group of 450 patients (250 female and 200 male) over a period of one year. All these patients had been in hospital for over one year, 50% for over five years, and 25% for over fifteen years (Table I). Patients with all types of mental illness were treated, except the large group of senile patients, dements suffering from advanced physical deterioration and almost continually confined to bed.

Table II indicates the age groups of the patients treated and is of interest for the fact that over 60% of the patients would, if the treatment were successful, be an asset to the community from the point of view of earning capacity.

Table III indicates that the treatment was directed to a wide selection of mental disorders and also that the schizophrenic-paraphrenic group represents two-thirds of the total. This particular group forms a large percentage of the patients in the chronic wards of all mental hospitals, and it is such patients who provide most of the violence, impulsiveness and generally erratic behaviour which are such a problem to the nursing and medical staff. This group was the first to be treated, the treatment being commenced with the most disturbed and later being extended throughout the wards, until finally in the refractory wards 80% of the patients came under the treatment.

Results were speedy and spectacular, and were critically checked by both of us during the early few weeks. Improvement in affect and behaviour occurred first, followed in favourable cases by improvement in ideation. Patients became less violent and more sociable, and began to take more interest in their surroundings and their personal appearance. Careful watch was kept for the occurrence of undesirable symptoms, particularly jaundice, which did not occur. The main symptoms were those of discomfort rather than illness—namely, local irritations of mucous membranes, photosensitization and somnolence.

TABLE I.
Length of Residence of Patients in Hospital.

Period (Years).	Treatment.			Total.
	Chlorpromazine.	Chlorpromazine and Reserpine.	Reserpine.	
1 to 2 ..	60	12	33	105
2 to 3 ..	38	5	30	73
4 to 5 ..	36	9	16	61
6 to 10 ..	41	9	16	66
11 to 15 ..	28	1	12	41
16 to 20 ..	35	3	15	53
21 to 25 ..	20	5	8	33
26 to 30 ..	8	0	2	10
Over 30	5	0	3	8
Total	271	44	135	450

The results of the treatment are indicated in Tables IV to VII. The headings 1, 2, 3 and 4 refer to the clinical improvement in ascending grades: 1, little or no improvement; 2, improvement definite; 3, improvement marked; 4, improvement to stage of leaving hospital.

No patient has been made worse by the treatment.

During the course of the treatment there has been a steady movement from group 2 to 3 and from group 3 to 4. Occasionally a patient in group 2 has, after months of treatment, suddenly improved greatly and moved to group 4.

TABLE II.
Age Groups.

Age (Years).	Treatment.			Total.
	Chlorpromazine.	Chlorpromazine and Reserpine.	Reserpine.	
Under 20 ..	4	1	3	8
Under 30 ..	33	5	19	57
Under 40 ..	46	12	33	91
Under 50 ..	64	10	38	112
Under 60 ..	59	9	25	93
Under 70 ..	45	5	13	63
Under 80 ..	19	2	4	25
Under 90 ..	1	0	0	1
Total	271	44	135	450

It is to groups 1 and 2, in which improvement to a certain degree has occurred and then failed to continue, that we are directing the use of "Pacatal", "Ritalin", "Frenquel" and "Meratran".

Groups 3 and 4 comprise 24% and 20% of the total respectively, and it is here that improvement has been marked, sustained and continuing.

One of the most interesting cases is that of the patient suffering from an obsessive-compulsive neurosis.

This forty-six-year-old woman, admitted to hospital in 1954, had for some years been impelled to wash her hands almost without cessation; and each time she used the

TABLE III.
Diagnosis.

Diagnosis.	Treatment.			Total.
	Chlorpromazine.	Chlorpromazine and Reserpine.	Reserpine.	
Schizophrenia ..	113	29	79	221
Paraphrenia	37	6	38	81
Affective psychoses:				
Manic	22	1	3	26
Mixed	1	1	1	3
Depressive ..	19	3	1	23
Congenital mental defect	22	0	3	25
Congenital mental defect with epilepsy	9	—	1	10
Epileptic psychosis	14	—	1	15
Dementia (arteriosclerotic) ..	18	1	6	25
Confusional psychosis	11	3	2	16
Dementia paralytica	3	—	—	3
Obsessive-compulsive neurosis	2	—	—	2
Total	271	44	135	450

toilet she would fill and choke it with paper, these symptoms being manifestations of guilt over a previous love affair. In spite of a good education she was completely impervious

TABLE IV.
Degree of Change for All 450 Patients.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	56	91	74	50	271
Chloropromazine and reserpine	16	19	6	3	44
Reserpine	24	45	30	36	135
Total	96	155	110	89	450

to psychotherapy, or indeed to any other form of therapy. She had, in fact, had courses of electroconvulsive therapy and full coma insulin without avail. Eventually she underwent bilateral prefrontal leucotomy, without any improvement whatsoever.

TABLE V.
Change in 221 Schizophrenics.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	34	30	31	18	113
Chlorpromazine and reserpine	15	9	3	2	29
Reserpine	15	29	14	18	79
Total	64	68	48	38	221

On admission to hospital she was in a pitiable plight—thin, emaciated and restless—and her continual handwashing and successful blocking of the ward toilets were a tremendous problem. She was a wretched, unhappy woman for whom there seemed no hope.

Her transformation following treatment with chlorpromazine was almost unbelievable. She became relaxed and happy and had a splendid appetite, gaining considerable weight, and she laughed at her former symptoms. After several months she proceeded on leave and obtained a position as a governess to some children.

It was surprising when this patient returned to the hospital with all her old symptoms in full force. On inquiry it was found that after seven months she had decided that she was so well that she no longer needed to take the tablets, and her relapse was the result of this decision. She has again been treated with chlorpromazine and has once again proceeded on leave.

TABLE VI.

Change in 81 Paraphrenics.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	1	11	19	6	37
Chloropromazine and reserpine	0	4	1	1	6
Reserpine	7	9	10	12	38
Total..	8	24	30	19	81

A male schizophrenic, aged twenty years, with inappropriate affective response and ideas of reference, failed to respond satisfactorily to electroconvulsive therapy and full coma insulin, and was approved by the Leucotomy Committee for operation in 1955. Pending arrangements for operation he was treated with reserpine and gradually improved to the extent of leaving hospital and remaining stable.

All other patients awaiting operation for leucotomy have been treated with chlorpromazine and reserpine and have improved to such an extent that leucotomy is not now considered necessary. (We are therefore of the opinion that before leucotomy is considered patients should have a full course of treatment by these drugs.)

TABLE VII.

Change in 52 Patients with Affective Psychoses.[1]

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	2	11	10	18	40
Chlorpromazine and reserpine	1	2	2	0	5
Reserpine	3	2	1	1	7
Total..	6	15	12	19	52

[1] This table is not divided into component manic, mixed and depressive phases as in Table III, because in cyclothymia the patient may change from one phase to another, and the diagnosis in our records depended on the patient's state on admission to hospital, not at the present time. But the patients were all considered to be suffering from affective psychoses.

In addition to the female patient mentioned earlier, a number of patients who had been leucotomized before admission to hospital have been treated, with favourable results.

The placing of the 20% of patients who are able to leave hospital has been, and still is, a difficult problem. Where there are friends and relatives who are still interested and have kept in contact with the patient over a period of years, the problem is relatively easy. It merely consists of correcting the previously unfavourable prognosis by substituting a more favourable one, by persuading relatives to take the patient home for a day, then for a week-end or two, and then on leave for twelve months, and allowing them to resume their former or other employment in six to eight weeks. We have followed the practice of keeping all these patients on leave for twelve months, so that we can keep contact with them and by frequent visits continue their psychotherapy. They are given prescriptions for the continuance of treatment with chlorpromazine or reserpine, but have to return in four to six weeks for renewal of the prescription and generally a reduction in dosage.

TABLE VIII.

Newly Admitted Patients: Age Groups.

Age (Years).	Treatment.			Total.
	Chlorpromazine.	Chlorpromazine and Reserpine.	Reserpine.	
Under 20 ..	5	1	5	11
Under 30 ..	37	6	24	67
Under 40 ..	42	3	39	84
Under 50 ..	36	7	18	61
Under 60 ..	20	2	12	34
Under 70 ..	19	—	8	27
Under 80 ..	12	—	2	14
Under 90 ..	2	—	—	2
Total ..	173	19	108	300

In a number of cases difficulty has occurred in persuading relatives to give the patient a trial away from hospital. The absence of the patient from the family circle for a number of years has led, in some cases, to the formation of extramarital attachments and a consequent reluctance to resume the former relationship. Where there are growing children, some have been informed that their mother is dead or that she will never return to the family circle. Where an unpleasant delusional symptom has been apparent for years and has suddenly ceased to express itself as a result of treatment, there is much diffidence about returning the patient to the family circle. The following case is a good example of this.

TABLE IX.

Newly Admitted Patients: Diagnosis.

Diagnosis.	Treatment.			Total.
	Chlorpromazine.	Chlorpromazine and Reserpine.	Reserpine.	
Schizophrenia	36	8	61	105
Paraphrenia	16	2	26	44
Affective psychoses:				
Manic	53	3	9	65
Mixed	—	—	—	—
Depressive	29	4	3	36
Congenital mental defect	3	—	1	4
Congenital mental defect with epilepsy	—	—	—	—
Epileptic psychosis ..	—	—	—	—
Dementia	11	1	2	14
Confusional psychosis ..	18	1	6	25
Obsessive neurosis ..	6	—	—	6
Anxiety neurosis	1	—	—	1
Total	173	19	108	300

A female patient, aged forty-six years, was admitted to hospital six years ago suffering from paraphrenia. Her most prominent symptoms were of voices accusing her of sexual immorality and perversions, and of sexual interference at night. This had been complained of by her in her home and in the presence of her husband and children, and had led to her removal to a mental hospital. Whilst in hospital her condition proved resistant to electroconvulsive therapy, as is the case with many paraphrenics. She

frequently wrote me plaintive letters requesting that her persecution by indecent language and behaviour should be prevented. It can easily be realized that she was a querulous, anxious and antagonistic patient.

After her steady improvement on reserpine therapy the question of her trial at home for a week-end came under consideration. In view of her past behaviour at home in front of the children her husband refused to consider the proposition, but under pressure consented that she should spend week-ends with her parents, stipulating that she should have no contact with her children. Fortunately, after a few week-ends he consented to give her a trial in her own home, a step which was attended with most favourable results. She has now been home for several months and visits us regularly for interview and gradual reduction of her medication.

TABLE X.

Newly Admitted Patients: Degree of Change for all 300 Patients.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	19	34	40	80	173
Chlorpromazine and reserpine	2	3	4	10	19
Reserpine	11	18	24	55	108
Total..	32	55	68	145	300

Where the patient has no relatives or friends the problem of placing the patient is more difficult and there is at present in New South Wales only the After-Care Association able and willing to provide the necessary accommodation for the patient whilst employment is found.

The improvement of such a large number of patients gives rise to a problem of rehabilitation both within the hospital and without, and requires an extension of hospital vocational training together with an investigation by trained rehabilitation officers.

TABLE XI.

Newly Admitted Patients: Changes in 105 Schizophrenics.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	2	6	7	8	23
Reserpine	8	13	20	41	82
Total..	10	19	27	49	105

Vocational rehabilitation may come into the mental hospital for the first time. The patient who is improved, freed of all restraints and friction with his fellows, is still not well. Old and useless habit patterns of years' standing need to be replaced by new ones, and a new orientation to the world outside the hospital is required if the patient is to adjust himself satisfactorily. Thus extra attention is needed from the occupational therapy department, from the social workers and from outside bodies who can reeducate the patient into useful channels.

The aspect of the hospital has so altered under these treatments that the nursing staff here had to readjust themselves to changing conditions. It is to their credit that they have done this; indeed, the treatment of so many patients would not have been possible without their interest and cooperation. Is it too much to expect the medical profession to readjust its attitude to the mental hospital, to realize that persons mentally ill are treated, that newer treatments have been available to them, and that research into prevention, causation and treatment is continuing, but that such investigations require a steady stream of new recruits?

Two pertinent questions may be asked regarding these newer drug treatments: (i) How long must treatment be continued? (ii) How far is treatment curative?

In answer to the first question, those patients remaining in hospital, as well as those on leave, have been slowly and steadily reduced to a maintenance dose, in some cases as low as 25 milligrammes of chlorpromazine and 0·5 milligramme of reserpine daily. A few in-patients and more patients on leave have ceased taking the drugs. How long medication must be continued cannot be stated at present. It may be that stability is only obtained on a maintenance

TABLE XII.

Newly Admitted Patients: Change in 44 Paraphrenics.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chlorpromazine	2	3	3	4	12
Reserpine	5	5	5	17	32
Total..	7	8	8	21	44

dose, as with anticonvulsants in epilepsy, with liver in pernicious anæmia or with insulin in diabetes.

As to how far treatment is curative, we would point out, as mentioned earlier, that we have kept patients on leave up to a period of twelve months to observe the progress of the patients in the home environment and have noticed no deterioration in their condition up to the present. A significant fact has emerged, that whilst approximately 15% of patients on convalescent leave return to hospital, this has not occurred amongst patients receiving chlorpromazine or reserpine, except in a few cases in which the patient ceased treatment of his own volition.

TABLE XIII.

Newly Admitted Patients: Change in 101 Patients with Affective Psychoses.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
Chloropromazine	7	10	24	44	85
Chloropromazine and reserpine	—	—	—	2	2
Reserpine	1	1	2	10	14
Total..	8	11	26	56	101

While the layman and the persons responsible for budgeting may ask "How many patients can you get out of the hospital?", this is not so important a question when one considers that a more important object of treatment is to make life more pleasant and more livable for those patients who will have to remain in hospital for the rest of their days.

If we are to accept the statement of Dr. Cunningham Dax, Mental Hygiene Authority in Victoria, that "every patient redeemed from a mental hospital saves the community more than £30,000", then this treatment has already justified itself from the financial aspect.

The tables previously presented to you indicate the results in cases previously regarded as chronic.

For purposes of comparison a series of tables (Tables VIII to XIII) is submitted, giving results for newly admitted patients. These tables cover a series of 300 patients (150 female and 150 male) admitted to hospital during the last twelve months. The results in schizo-

phrenia and paraphrenia, approximately 50% in each disease, are more favourable than those obtained with any other method of treatment in our experience. The figures in affective psychoses are not so favourable at present as with electroconvulsive therapy, but the disadvantages of this method of treatment are avoided. As in the previous tables, there is a continual shift of persons from group 3 to group 4.

It is not claimed that these drugs, either singly or combined, are a cure for mental illness. They have had outstanding success in the control of psychomotor overactivity and psychotic tension. The deteriorated schizophrenic, the aggressive paraphrenic and the boisterous manic are alike calmed. The atmosphere of the chronic wards in a mental hospital has been changed as no other method of treatment has ever done. Restraint, destructiveness and violent behaviour have disappeared. Previously disturbed patients have been able to mix equally with convalescent patients in occupation, recreation and the company of relatives and friends.

We feel that chlorpromazine should be given a trial before electroconvulsive therapy is instituted, because of the sometimes unpleasant complications of that treatment.

From our experience we feel strongly that these drugs should be given a full trial before leucotomy is considered.

These drugs, together with "Pacatal", "Ritalin", "Frenquel" and "Meretran" (see Table XIV), which time will not permit me to discuss and on which our investigations are not yet complete, are a valuable addition to the armamentarium of the psychiatrist.

TABLE XIV.
Results of Treatment with Other Drugs.

Treatment.	Degree of Change.				Total.
	1	2	3	4	
"Pacatal"	9	7	13	17	46
"Frenquel"	7	3	8	4	22
"Meratran"	5	6	9	12	32
"Ritalin"	1	5	10	9	25
Total..	22	21	40	42	125

May I conclude with a quotation from Cattell (1934), who refers to the processes of the mind as "a region of unexampled complexity, of baffling obscurities and formidable resistances which at present is left to a mere handful of pioneers. It is like a long battle-line, thinly held, awaiting reinforcements. When society sends these reinforcements we can rest assured of advances which will change the whole face of social life and contribute in an unprecedented degree to human happiness and effectiveness."

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INDUCTION OF LABOUR BY THE INTRAVENOUS DRIP ADMINISTRATION OF "PITOCIN".

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THE purpose of this paper is to illustrate the uses and pitfalls of the administration of "Pitocin" by the intravenous drip method. This procedure was first described by Theobald *et alii* (1948).

During the year ending July 1, 1955, there were 3513 confinements at King Edward Memorial Hospital for Women. Eighty-two of these patients received "Pitocin" by the intravenous drip method, used either for induction of labour or for treatment of uterine inertia. This number represents 1·36% of private patients treated, and 3·24% of public patients.

Method of Administration.

"Pitocin" is administered as follows. Two flasks, each containing 500 millilitres of 5% dextrose solution, are set up in parallel on an intravenous drip stand, and connected above a drip chamber by a Y-tube. To one flask five units of "Pitocin" are added. After insertion of an intravenous needle, the "Pitocin" solution is allowed to flow into the ante-cubital vein, at a maximum rate of 20 drops per minute.

The patient is kept under continuous observation by a medical officer, or senior sister, and a careful and accurate record is made of the frequency and duration of contractions, fœtal heart rate, maternal pulse rate and blood pressure. The rate of flow is increased or decreased according to the contractile response of the uterus. When regular rhythmic contractions have become established, with a duration of about thirty seconds, and an interval of less than five minutes, the "Pitocin" solution is clipped off, and the 5% dextrose solution is allowed to run in slowly.

If the contractions subside, the "Pitocin" solution is again run into the vein. When one is satisfied that they are properly established, after an arbitrary period, the drip may be stopped. It is preferable that it be allowed to run for the greater part of the first stage of labour, and may even be continued into the second stage. Dilatation and effacement of the cervix should be confirmed by rectal or vaginal examination before the drip apparatus is removed.

The observer is required to stop the flow of "Pitocin" solution whenever there is any indication of prolonged or tonic uterine contraction, irregularity of the fœtal heart, maternal shock, or pain in the abdomen or back, other than labour pains.

The advantage of this double flask method is that the flow of "Pitocin" solution can be discontinued or recommenced at will, without the need to remove or reinsert the intravenous needle.

The foregoing procedure is frequently preceded by artificial rupture of the membranes.

The procedure is much the same when a drip administration of "Pitocin" is used in the treatment of the atonic type of uterine inertia, when there is no evidence of disproportion.

Analysis of Cases.

Twenty-eight of the patients who received "Pitocin" drip therapy were *primigravidæ*, and 54 were *multigravidæ*. The procedure was associated with surgical induction of labour in 52 cases (63·4%).

The most common indication was for induction of labour in preeclampsia (31 cases). "Pitocin" drip therapy was also administered for induction of labour in eight cases of post-maturity, and in 16 cases of Rh incompatibility. It was given in five cases in which an earlier artificial rupture of the membranes (with or without medical induction with "Pitocin" injections) had failed, and in five cases of premature spontaneous rupture of the membranes.

The other indications were as follows: intrauterine death (five cases), eclampsia (two), fœtal abnormality (two), unstable "lie" (one), pyelitis (one), bad obstetrical history (two), ante-partum hæmorrhage (three), diabetes (one). Only one patient with uterine inertia was treated. In five cases (6·1%), the "Pitocin" drip therapy was considered to have failed. One of these was eventually discovered to be ectopic pregnancy at term. The fœtus was dead. In another case, the first "Pitocin" treatment (administered for premature rupture of the membranes) was unsuccessful, but a subsequent one was successful. If these two

cases are excluded, the failure rate was 3·7%. In one patient with chronic nephritis, labour was eventually induced successfully at twenty-six weeks' gestation with a rectal tube, after a drip administration of "Pitocin" had failed. One patient, considered to be doubtfully in labour, received "Pitocin" by the drip method, but the contractions subsided, and she was eventually delivered after a spontaneous labour two weeks later.

The longest induction-delivery interval was fifty-five hours, and the shortest one hour. The average interval was 13·4 hours.

Five patients required forceps delivery. This is an incidence of 6%, which does not differ greatly from the overall rate for the hospital (6·6%). Apart from the one undelivered patient, and the ectopic pregnancy in which delivery was effected by laparotomy, the remaining cases were normal vertex deliveries. There were seven post-partum hæmorrhages in the series—an incidence of 8·5%. The incidence of post-partum hæmorrhage among all patients delivered in the hospital over the same period was 7·7%. If anything, it would appear that stimulation of the uterus by "Pitocin", in induction of labour, may cause a slightly higher incidence of uterine atony in the third stage, and that the prophylactic administration of oxytocic drugs during this stage would be advisable.

Mortality.

Fourteen infants died. At first glance this may appear to be high, but the cause of death was generally the condition for which the "Pitocin" drip therapy was given. In five cases it was administered for ante-partum fœtal death, and a sixth case was the ectopic pregnancy already mentioned. One stillbirth was due to *hydrops fœtalis*. Two more stillbirths, and two neonatal deaths of premature babies, were due to severe preeclampsia, and two neonatal deaths were due to fœtal abnormalities. One neonatal death occurred in a case in which labour had been induced at twenty-six weeks' gestation, for chronic nephritis.

One stillbirth may have been partly due to the "Pitocin" drip therapy.

Labour had been induced, as the patient, pregnant for the third time, was eleven days past the expected date of confinement and had been gaining weight excessively. The fœtal heart rate was normal and regular up to forty minutes before parturition, when it was no longer recorded. The duration of labour was just over two hours, and the baby was born cyanosed, with the cord wound tightly around its neck. The post-mortem report indicated that death was due to asphyxia. It is difficult to assess how much of this was due to the "Pitocin" drip therapy and rapid labour, and how much to the cord around the baby's neck.

The other complication attributed to the "Pitocin" drip therapy was of a more serious nature.

This patient, aged forty-three years, pregnant for the fifth time, had severe essential hypertension, with superimposed preeclampsia, and a mild accidental hæmorrhage. After external cephalic version of a fœtus presenting by the breech at thirty-six weeks' gestation, labour was induced by artificial rupture of the membranes, and "Pitocin" drip therapy. As the first flask of "Pitocin" solution did not excite any regular contractions, the administration of a second flask was commenced. While this was running, the patient suddenly became shocked, and died, undelivered, shortly afterwards. Post-mortem examination revealed that the uterus had ruptured over the posterior wall of the lower uterine segment. There was little blood loss, and death was presumably due to shock. The patient also had an enlarged heart.

Comments.

It would appear that induction of labour by intravenous drip administration of "Pitocin" is a very useful procedure, successful in a high percentage of cases, but with certain risks, against which we must guard.

The full-term ectopic pregnancy, in which an attempt was made to induce labour by intravenous drip administration of "Pitocin", indicates that such abnormalities must first be excluded.

The dangers to the fœtus as a result of prolonged, tetanic, or excessively strong uterine contractions are obvious, and one must avoid these by careful observation of the patient, and control of the rate of flow of the drip. If the contractions become excessive in frequency, strength or duration, or if there is any indication of fœtal distress, the flow of "Pitocin" solution must be stopped immediately. In our case of intrapartum fœtal death, despite the cord around the neck of the fœtus, the rapidity of labour and strong uterine contractions due to the "Pitocin" cannot be excluded as a contributing factor to its death.

Although several factors contributed to the maternal death in our series, the "Pitocin" drip therapy played a most important part. Owing to the risk of coronary artery constriction from even small quantities of pitressin, which may be present in "Pitocin", the use of this drug is undesirable in the presence of cardiac enlargement and hypertension. Shock following rupture of the uterus would be sufficient to cause sudden death in these circumstances. Lesser and Eason (1954) describe the death of an anæsthetized patient from cardiac arrest, during induction of labour by "Pitocin" drip therapy. The concentration of "Pitocin" used was 30 units per litre. These authors point out the dangers of administering "Pitocin" by the drip method in combination with anæsthesia—particularly cyclopropane—and recommend that it should be avoided in the treatment of patients aged over forty years, and of those who have coronary artery disease.

According to Holland (1955), "Pitocin" has caused many uterine ruptures. It should not be given if the head is not engaged, if there is any disproportion, or if there is a breech presentation. It is unwise to give "Pitocin" to women who have had over four previous labours, or who are aged over thirty-five years. High multiparity and advanced age of patients are the two most important factors in spontaneous rupture of the intact (non-scarred) uterus. Parker and Roberts (1954) state that the presence of a scar in the uterus is a definite contraindication to the use of "Pitocin". Stone *et alii* (1955) consider the main contraindications to "Pitocin" drip therapy to be grand multiparity and absolute disproportion, but maintain that the treatment is not contraindicated in twin pregnancies or breech presentations, or for patients with elevated blood pressure.

In our case the patient was elderly and had had more than four previous labours, and the presenting part was not engaged, so that "Pitocin" administration was contraindicated. The administration of a second flask of "Pitocin" solution was undesirable. Parker and Roberts (1954) and Faris and Kahlenberg (1954) recommend the use of intravenous "Pitocin" drip therapy for the induction of labour in patients with preeclampsia, particularly those with "unripe" cervices. The last-mentioned authors also favourably discuss the use of the treatment in cases of uterine inertia, in which it may be continued into the third stage of labour.

Stone *et alii* (1955) have observed a large series of cases in which "Pitocin" was used intravenously for induction of labour, or to supplement it. Their failure rate in induction of labour was 6·6%. They found that artificial rupture of the membranes was not essential, but that this procedure did enhance the success of the treatment.

Carey (1954) describes an elaborate technique for induction of labour in preeclampsia. The effects of an intravenous drip administration of "Pitocin" are gauged by recording the intrauterine pressure and varying the rate of flow of "Pitocin" solution accordingly. The intrauterine cannula used also cleverly serves for the introduction of an antibiotic into the uterus.

Summary.

The method of administering "Pitocin" by the intravenous route for induction of labour has been described. A series of 82 patients treated in this way has been analysed, and particular reference has been made to a maternal death as a result of rupture of the uterus. The indications for and contraindications to "Pitocin" drip therapy are discussed, and reference is made to the literature on this subject.

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THE MATURATION FACTOR IN ENURESIS.

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AND

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PREVIOUS communications have drawn attention to the relationship between early and strict toilet routines in infants and the subsequent emergence of enuresis (Bostock and Shackleton, 1951, 1952). Those observations were based on two series of patients. The first series consisted of 73 children, of whom 29 were enuretic, investigated at the Lady Gowrie Centre. The second series consisted of 73 children at the Brisbane Children's Hospital, of whom 36 were enuretic. The present communication deals with a third series of a further 41 cases of enuresis drawn largely from the Child Guidance Clinic of the Brisbane Children's Hospital. It is presented as shedding further light on the significance of toilet training.

Each of the 41 enuretic children was checked by X-ray examination, analysis of the urine, and physical examination to exclude an organic cause. The standard for the diagnosis of enuresis was the involuntary passing of urine during sleep into the bed, at least three times per week. The number of children was made up of 24 boys and 17 girls, and their ages ranged from four to twelve years. Eleven had the pattern of the enuretic dyad. The remainder were consistent enuretics and had never been dry. Of the children in this series, 35 had had early toilet training. Rigidly strict training was admitted by the parents in 29 cases. Many mothers admitted to having been irritable at "potty" delays and to having used such active measures of coercion as slapping. On the other hand, there were six cases in which the early training was undoubtedly conducted with gentleness. In the remaining six cases no effort had been made to train the child.

Is Rigid or Early Training the Chief Factor?

In our comments on the first and second series accent was placed on the severity and rigidity of the early toilet training. While the present series substantiates the frequency of rigid training, the existence of a group in which early training was gentle forces consideration of an alternative interpretation. The rigid training may be coincidental; the disturbing element leading to the subsequent enuresis may be the earliness of the training routine. Our attention to this possibility has been gradually developed through study of racial cultures in which training is left "to nature" without producing evidence of frequent enuresis. It would seem that two or three years are required to produce adult types of urinary and defæcatory coordination.

The problem is to decide whether an attempt to cut down the toilet training time drastically in itself could be such a disturbing factor as to produce an interference with the normal process of maturation.

The Psychological Approach.

It must be conceded that whether early toilet training is either rigid or gentle there is in both an element of frustration. The baby is being expected to achieve the unnatural and to sit on the pot, a position which to the child is neither satisfying nor interesting. Frustration without pain is a common experience. Most people can testify to the frustration which accompanies an enforced attendance at dull meetings, bouts of strap-hanging in public vehicles, or waiting for an overdue appointment. A classical example of frustration occurs in Pavlov's dogs, who, when denied food which they expected, fell asleep. It is significant that deep sleep in enuretics has frequently been observed. In this resepct it may be noted that treatment by sleep-reducing drugs, such as amphetamine or ephedrine, has often been described. A reaction to a frustrating or hostile stimulus is aggression. This has been shown experimentally by numerous observers. Latent hostility and aggressive traits frequently occur in enuretics.

Psychoanalytical Approach.

Psychoanalytical literature supports the idea that enuresis is part of considerable resistance to interference with a natural process, and it is regarded as a manifestation of urethral aggression. The urethra becomes cathected, at a certain stage in the psychological development of the child, as an element in an early organ language. Thereby the self makes articulate primitive emotional responses. According to Ella Freeman Sharpe (1940):

> When . . . this achievement of bodily control . . . becomes automatic, the emotions of anger and pleasure which heretofore accompanied bodily discharges must be dealt with in other ways.

The persistence of enuresis suggests that an immature pattern of emotional expression has been retained by the individual. With reference to this point, Felix Deutch (1939) infers that the psychosomatic symptoms become the unconscious expression of the conflict, "enuresis emerging as an organ language antedating and supplanting more overt expressions of emotion". He goes on:

> In order for this to be the case, the organ, or one of its functions, must have been involved in the psychosomatic process at a very early time. The rigidity of the symptom depends on the time factor, because the function of the organ must have a significance at a given time which is conducive to its formation.

Melanie Klein (1937) quotes instances in which she found that urination was an expression of aggression against the parents. Sadistic phantasies directed against them were said to accompany the act. Are not such psychoanalytical findings in keeping with those of our own observation? The world of an infant is a strange world, in which food and excreta loom so large that they play an enormous part in the joys of brief periods of a day filled largely with sleep. It would be surprising if interference forcing the orderly integration of such patterns into more adult living did not have side effects. We suggest that one of these is an interference with bladder control in sleep. This results in enuresis.

Practical Consideration.

The foregoing considerations have more than an academic interest, in that the ætiological approach is a guide to therapy. There has been a tendency in the past to regard enuresis as an entity for which rule-of-thumb methods should be employed in treatment. It would seem that many factors are involved and that in future adequate treatment will be based on the individual aspects of each case. Not the least will be that of assessing the degree of interference with normal maturation. There may be present an immaturity of adaptation involving far more than a mere urinary symptom. Interference with many pathways in the pattern of living may be present, including

difficulties in other psychosomatic fields, in interpersonal relationships and in attitudes towards parents. The scope of therapy will be enlarged through giving due attention to this much wider field of maladjustment.

In the field of prophylaxis the implication is clear. We must not attempt to overhasten the time-table which nature has evolved for the maturation of urinary control.

Summary.

1. An observation was made of 41 enuretic children, of whom 35 had had early toilet training.

2. It is suggested that the main ætiological factor in this condition may not be a rigid toilet training routine *per se*, but rather interference with the time-table which nature has evolved for maturation of urinary control.

3. The practical implications of this are discussed.

Acknowledgements.

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SPONTANEOUS INTRACRANIAL HÆMORRHAGE: A CLINICO-PATHOLOGICAL REPORT.

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BY spontaneous intracranial hæmorrhage it is implied that external trauma played no part or was insignificant in the history of the disease. In this sense, the condition was responsible for one in every 16 deaths in Victoria in 1951.

The reason for this study is that the mortality of medically treated patients is so high (60% to 70%) that any surgical endeavour aimed at reducing this mortality is to be encouraged. However, it is realized that operation may not prove to be the only method of treatment, and that the final aim of all medical treatment is prevention. This may yet be within the realms of possibility for hypertension and atheroma, and even for congenital malformations.

Material.

This report is based on 905 consecutive autopsies performed at the Alfred Hospital over a period of twenty months from April, 1953. In this group there were 105 cases of spontaneous intracranial hæmorrhage, or nearly one in nine. The Alfred Hospital is a 430-bed general teaching hospital, and as such accepts all types of non-infectious medical and surgical cases; however, over the period under review a shortage of beds prevented the admission to hospital of all patients suffering from cerebral hæmorrhage, and so it is probable that admission was favoured by comparative youth, a normal blood pressure, and the absence of focal signs, or indeed any combination of signs or symptoms which may have suggested tumour.

Method of Examination.

With the exception of certain cases in which the brains were dissected in the fresh state in attempts to discover the bleeding point, all brains were perfused with buffered 10% formalin solution and suspended by the basilar artery in the same solution for two to four weeks. Usually histological examinations were made.

Findings.

The cases (see Table I) have been grouped according to the primary site of hæmorrhage, as follows: intracerebral, 44; subarachnoid, 38; intracerebellar, eight; pontine, seven; subdural, six; intraventricular, two.

TABLE I.

Site.	Number of Subjects.	Sex.		Average Age (Years).	Subjects with Hypertension.
		Male.	Female.		
Intracerebral ..	44	23	21	54	36
Subarachnoid ..	38	14	24	55	17
Intracerebellar	8	3	5	64	7
Pontine ..	7	4	3	64	7
Subdural ..	6	2	4	60	5
Intraventricular	2	1	1	40	1
Total ..	105	47	58	—	72

Primary Intracerebral Hæmorrhage (44 Cases).

The ages of patients ranged from seventeen to seventy-eight years, with an average of fifty-four.

There were 23 male patients and 21 females.

The part played by hypertension was important, and there was a history of this in 36 cases. Of the remaining eight subjects, two had leuchæmia (the two youngest in the series); one had acute bacterial endocarditis; two had enlarged hearts at autopsy, which may mean that the patients concerned had hypertension, although no history of this was obtained. In the other three only the brain was examined at autopsy. In four cases there was a history of a previous "stroke". Three patients were taking hypotensive drugs ("Vegolysin") at the time of hæmorrhage, their ages being twenty-eight, thirty-four and fifty years.

The average period of survival after the onset of symptoms was three to four days; however, 32 patients died in the first two days. The shortest survival was a few hours, and the longest five weeks.

In three subjects there was no blood in the cerebrospinal fluid. In two of these there were localized collections of blood confined to the brain substance; however, in the third, who died shortly after lumbar puncture, the hæmorrhage had entered the ventricle.

Pathology: The site of hæmorrhage at autopsy is shown in Table II.

TABLE II.

Site.	Number of Subjects.	Side.	
		Right.	Left.
Basal ganglia and external capsule ..	34	13	21
Thalamus	4	1	3
Parietal lobe	1	—	1
Frontal lobe	1	1	—
Internal capsule	1	—	1
Bilateral basal ganglia	1	—	—
Multiple sites (leuchæmia)	2	—	—

In 38 cases the hæmorrhage had ruptured into the ventricles or through the surface, and in 12 of these there was an associated brain-stem hæmorrhage. In one case an intracerebellar hæmorrhage was also present. Two were associated with unruptured aneurysms of the circle of Willis.

[1] Assisted by a grant from the E. H. Flack Research Fund.

Atheroma was present in 31 cases, mainly in subjects aged over forty years.

Despite a careful search in several fresh specimens, no bleeding point was found. In a few there was evidence of old infarction at the edge of the hæmorrhage, and in many cases ring hæmorrhages surrounded the main clot.

Discussion.

These cases bear out the statement by Fisher (1953) that "primary intracerebral hæmorrhage should not be diagnosed in the absence of hypertension". As the bleeding vessels are of small calibre, it is unlikely that atheroma plays any direct part in the process of rupture, particularly as in most of the younger hypertensives there was no evidence of atheroma in the larger arteries at the base of the brain.

Primary Subarachnoid Hæmorrhage (38 Cases).

In 35 cases an easily recognized aneurysm had ruptured. Of the remaining three, no bleeding point could be found in two cases despite the presence of a considerable amount of subarachnoid blood. In the other case there was a hæmangioma of the temporal bone (possibly a jugular body tumour).

Ruptured Aneurysm (35 Cases).

The average age of these patients was fifty-five years, ranging from fifteen to seventy. There was only one death under the age of thirty years.

There were 13 male subjects and 22 females.

As with the intracerebral group the onset usually occurred during the day time whilst the patient was engaged in activity.

Hypertension was present in 16 cases, in one this being associated with polycystic kidneys. Another of this group was taking hypotensive drugs ("Vegolysin").

In half of the cases death followed what was believed to be the first rupture. Hypertension was present in 11 of these. Fourteen patients had recurrent hæmorrhages in hospital, and in ten of these cases the interval was a week or less. One patient had a twenty-year history of oculomotor palsy on the same side as the aneurysm, the oculomotor nerve being involved in its capsule. Another had a history of previous hæmorrhage fifteen years before death.

During life cerebral angiography was used to display the aneurysm in 19 cases, no angiographic examination being performed in the others.

All the aneurysms in this series were saccular and occurred at the junctions of arteries of the circle of Willis or its main branches (see Table III).

TABLE III.

Site of Ruptured Aneurysm.	Number of Subjects.	Side.	
		Right.	Left.
Anterior cerebral with anterior communicating	13	—	—
Internal carotid with posterior communicating	15	12	3
Middle cerebral, first major bifurcation	4	3	1
Basilar bifurcation	2	—	—
Posterior cerebral with posterior communicating	1	1	—
Total	35	16	4

In eight cases the aneurysms were multiple (two aneurysms in five cases and three in three others).

Atheroma was a prominent feature in 23 cases, and in a number of these histological preparation showed atheroma in the wall of the aneurysm.

In 30 of the 35 cases there was complicating damage to the brain. Bleeding into the brain substance occurred in 25, and in 13 of these blood had entered the ventricles. In six brain-stem hæmorrhage also occurred. Cerebral thrombosis was a complicating factor in three cases, subdural in one and cerebral "œdema" in one.

Anomalies of the circle of Willis were common, particularly in the region of the anterior communicating artery, where there was frequently a network of communicating vessels. In one case there was a persistent basilar-carotid anastomosis.

Discussion.

The ætiology of saccular aneurysms is still not clear. On the one hand they have been attributed to congenital defects in the arterial wall, and on the other to degenerative changes. In this series hypertension appears to have been an important aggravating factor. There have been several case reports of cerebral aneurysm associated with polycystic kidneys or coarctation of the aorta. However, it is difficult to say whether these aneurysms were primarily congenital in origin or due to hypertension from an early age.

The age of occurrence was much the same as in the primary intracerebral group. Only one patient died who was aged under thirty years, and this was in keeping with the number of hospital admissions in this age group over the same period—namely, three.

The high incidence of complicating cerebral damage was a feature which has already been stressed by Robertson (1949).

In passing, it was of interest to note that of the aneurysms not in the mid-line 16 were on the right side and four on the left.

Intracerebellar Hæmorrhage (Eight Cases).

The youngest subject was aged fifty-nine years, the oldest seventy-five.

Three subjects were males and five females.

Hypertension was present in seven of the eight cases. Signs of cerebellar disturbance were present in most patients. In five death occurred within thirty-six hours of the onset of symptoms. In one there was no blood in the spinal fluid at lumbar puncture; and at autopsy the hæmorrhage was localized in the cerebellar tissue.

The site of hæmorrhage was the lateral lobes in seven cases and the mid-line in one (four on the right, three on the left). In six cases the hæmorrhage had entered the fourth ventricle or ruptured on to the surface of the cerebellum.

Pontine Hæmorrhage (Seven Cases).

The age of the youngest subject was fifty-five years, the oldest seventy-six years.

Three subjects were females and four males.

All subjects had hypertension, and all had atheroma of the cerebral arteries. Two patients had a history of a previous "stroke", and another was taking hypotensive drugs. All died within six days of the onset.

In five cases blood had entered the fourth ventricle. In one there were unruptured aneurysms on both middle cerebral arteries; an old infarct was present in another.

Subdural Hæmorrhage (Six Cases).

The age range was thirty to seventy years, the youngest patient being the only one aged under fifty years.

Two subjects were males and four females.

Hypertension was present in five subjects, including the youngest in the group. There was no history of trauma in any case. Headache, usually severe, was the outstanding feature of the illness. Operation was undertaken in all but one case. However, at the time of operation all patients showed signs of a brain-stem lesion.

The average survival period from the onset of symptoms was eight days, ranging from one to fifteen.

The subdural collection of blood was situated over the parietal region in all cases. In one case it was bilateral, in four on the left and in one on the right. There was a small amount of subarachnoid blood in one case, and possibly this was the primary site of bleeding.

Brain-stem hæmorrhage complicated five cases, and in one of these infarction over the posterior cerebral artery field was also present.

Histological examination showed the presence of granulation tissue to a depth of about 0·5 centimetre in one case, with a five-day history from the onset.

Discussion.

Clinically these patients ran a subacute course, and hypertension was a prominent feature in five. The absence of a history of external trauma was noteworthy.

In all but one case death could be attributed to secondary brain-stem hæmorrhage. This is a frequent complication of supratentorial lesions, whether hæmorrhage or neoplasm, and has been reported before by Cox (1939), and earlier by Moore and Stern (1938).

Intraventricular Hæmorrhage (Two Cases).

In one sbject, a male, aged fifty-three years, there was a history of hypertension, but no bleeding point was found. The other subject was a normotensive male, aged thirty-four years, in whom an arterio-venous malformation around the brain-stem was found at autopsy. This had been noted by angiography and declared inoperable.

Conclusions.

During the period under review approximately two-thirds of the patients admitted to hospital with spontaneous intracranial hæmorrhage died in hospital. The mortality was highest with primary hæmorrhage into the brain substance (pons, cerebrum and cerebellum) and lowest in the subdural hæmorrhage group.

Hypertension was practically always present in patients with primary hæmorrhage into the brain or subdural space. In the subarachnoid group hypertension was present in approximately half of the patients, and its presence had an unfavourable effect on the immediate prognosis. Whilst the absence of hypertension virtually precludes a diagnosis of primary intracerebral hæmorrhage, in the absence of blood dyscrasia, its presence does not exclude subarachnoid or subdural hæmorrhage.

The age of occurrence in the primary subarachnoid and in the primary intracerebral groups was approximately the same (see Figure I).

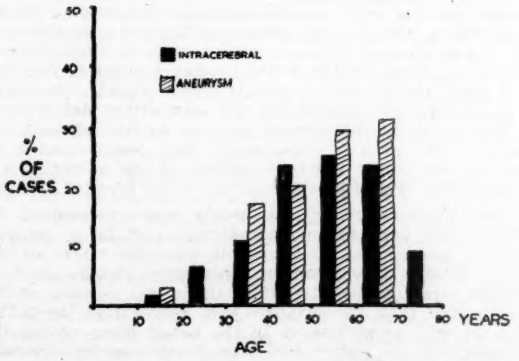

FIGURE I.

Showing the age relationship between deaths due to primary intracerebral hæmorrhage and those due to ruptured aneurysm.

Secondary brain-stem hæmorrhage was common in supratentorial lesions, and its presence precludes a satisfactory outcome in surgically treated patients.

Summary.

In 905 consecutive autopsies there were 105 cases of spontaneous intracranial hæmorrhage. The main clinico-pathological findings are presented.

Acknowledgements.

I am grateful to Dr. A. V. Jackson and his staff for their cooperation in this project. Dr. L. B. Cox has given valuable advice throughout.

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Reports of Cases.

TOTAL PELVIC EXENTERATION IN THE TREATMENT OF RECURRENT CARCINOMA OF THE CERVIX.

By J. CAMERON LOXTON,
Sydney.

THE appearance of metastases following an extensive operation for eradication of cancer is a great disappointment to everybody concerned. The surgeon is confronted with the problem of what now is to be done for his patient. In the past he had to choose between the alternatives of doing nothing beyond simple palliation and the prescription of analgesic drugs, or of referring the patient for deep X-ray therapy. Unfortunately this all too often meant more or less the same thing. The difference, as far as the surgeon was concerned, was that in the latter case he had elected to hand over his responsibility to somebody else, and no longer would be confronted with the pitiful spectacle of his patient slowly dying from cancer.

In the past ten years, with a better understanding of physiology and the introduction of efficient biochemical control, a new and much wider field of pelvic surgery has been opened up. This followed the work of Alexander Brunschwig, M.D., and his associates at the Memorial Hospital for Cancer and Allied Diseases, New York. It is now possible to deal successfully with quite extensive cases of cancer in this region by complete removal of all the pelvic viscera, surrounding tissue and lymph nodes, provided, of course, that the disease has remained confined to the pelvis. The patient may then be returned to a more or less normal and useful life.

It is hoped that description of the following case, in which I performed total pelvic exenteration more than eight months ago, will serve to illustrate the main points.

Clinical Record.

Mrs. A., a married woman, aged fifty-six years, who had had one child and a miscarriage many years previously, was found to be suffering from carcinoma of the cervix. On May 4, 1953, a Wertheim's radical operation with removal of lymph nodes was performed by the late Dr. F. A. Maguire shortly before his death. Pathological examination revealed extensive infiltration of the cervix by squamous carcinoma, the cells being transitional in type, with mitotic figures described as scattered. No carcinoma was found in the lymph nodes.

Some fourteen months later a small recurrence, barely palpable, was found in the scar in the vaginal vault, and the diagnosis was confirmed by biopsy. This was treated on September 15, 1954, by the local application of a 2880

milligramme-hour dose of radium, and six weeks later, on October 26, 1954, most of what remained of the vagina was removed by a combined abdomino-perineal procedure.

After my return from the United States, where I had spent some time with Professor Brunschwig at his clinic in New York, this patient was found to have developed a further recurrence of the carcinoma, this time high up in the space between the bladder and the rectum, which formerly had been occupied by the vaginal vault.

FIGURE I.

Specimen after removal, cut in sagittal section, showing the growth above the vaginal stump and between the bladder and rectum.

On September 30, 1955, the diagnosis was again confirmed by biopsy. On this occasion, however, the obtaining of biopsy material was more than usually difficult owing to the relative inaccessibility of the nodule and the risk of damaging these structures. By this time the patient was in considerable distress from pelvic pain, dysuria and pain on emptying her bowels. She looked ill and had lost weight.

The only form of treatment which was likely to prove of value, and which offered any hope of permanent cure, now appeared to be total pelvic exenteration. Because of its high primary mortality and the necessity to institute a permanent "wet" colostomy, the position was fully explained and then put to the patient. After further consultation and consideration of the matter, she chose to submit to this operation, rather than to remain in the intolerable circumstances in which she now found herself.

Accordingly, on October 29, 1955, she was admitted to an intermediate bed in the King George V Memorial section of the Royal Prince Alfred Hospital. Investigations by excretion pyelography and blood urea estimation failed to reveal any involvement of the renal tract or impairment of renal function. The X-ray appearance of the chest was normal and the blood picture satisfactory. The alimentary tract was prepared by purgation on the third and second days prior to operation, and its bacterial flora controlled as far as possible by a four-day course of phthalylsulphathiazole, one gramme four-hourly, and streptomycin, one-half gramme by mouth twice a day for the final two days prior to the operation.

On November 2, 1955, with the patient under closed circuit general anæsthesia, with administration of relaxants and continuous blood transfusion, the abdomen was opened by a mid-line incision extending from the *symphysis pubis* to the umbilicus. The abdominal cavity was then explored without finding any evidence of metastases in the pelvic and aortic lymph nodes, omentum, liver *et cetera*.

As the practicability of the operation had now been established, uretero-colic anastomosis was performed as a preliminary to evisceration. This was carried out in the following manner. A broad strip of peritoneum overlying each ureter, including the latter, with its supporting areolar tissue and blood supply attached, was dissected out. The ureters on either side were divided at as low a level as possible. The descending colon was mobilized and a point selected on each side, at about its junction with the sigmoid colon at the pelvic brim. At these two points the lumen of the bowel was opened by stab wounds about one-third of an inch in length, passing directly through all layers of the bowel wall. The cut ends of the ureters were split longitudinally for about three-quarters of an inch. A portion measuring about one and a half inches of each ureter, together with its blood supply and areolar tissue, from which, however, the peritoneal flap had been reflected, was drawn through the stab wound on each side and fixed within the lumen of the bowel by stay sutures of fine silk at a point about one and a half inches distal. The walls of the ureters were sutured to the edges of the stab wounds in the colon by interrupted sutures of fine chromicized catgut. The area of anastomosis was finally sealed by suturing the lower reflected portion of the specially prepared strips of peritoneum over it, in the form of a patch.

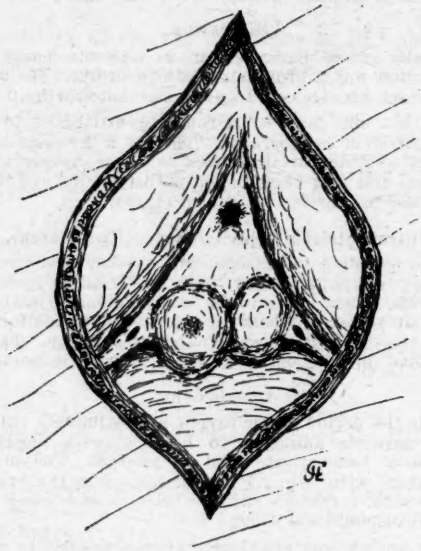

FIGURE II.

The bladder opened to show the growth beneath the trigone with commencing ulceration on the left side.

Total evisceration of the pelvis was commenced by raising the peritoneum and dividing it in a circular manner, the line of division following the curve of the pelvic brim. By dissecting anteriorly in the cave of Retzius, first the bladder, then the distal portion of the ureters and then the urethra were freed from the pelvic wall, as well as structures in the pelvic floor. Next, the parametrium on either side was divided as far laterally as possible, and the dissection carried posteriorly to expose the sacral plexus and free the sigmoid colon, rectum and anal canal, together with the endopelvic connective tissue and remaining pelvic lymph nodes.

The *levatores ani* and structures in the pelvic floor, together with the ischio-rectal pads of fat and the skin surrounding the vulva and anus, were divided in an elliptical manner by an incision which extended from the

symphysis pubis to the coccyx. The mass of pelvic viscera (see Figure I), consisting of the bladder, terminal parts of the ureters and urethra, the growth, the stump of the vagina, the sigmoid colon, rectum and anal canal, together with the entire pelvic peritoneum, the endopelvic connective tissue and the remaining pelvic lymph nodes, *levatores ani*, vulva, perineum, anus *et cetera*, were lifted out abdominally, leaving an aperture in the perineum as

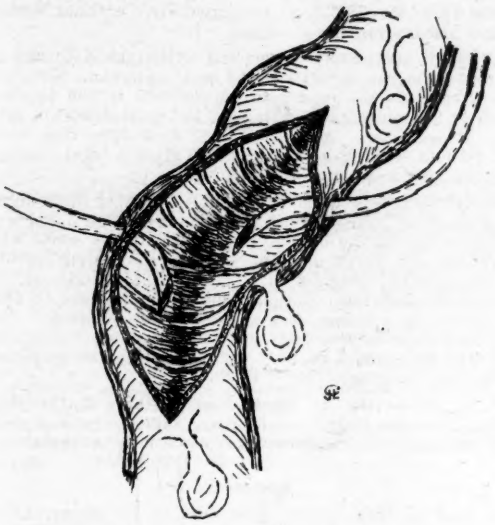

FIGURE III.
Final result of method of uretero-colic anastomosis.

large as a fœtal head. After the various bleeding points had been attended to, the pelvic cavity and aperture in the perineum were packed with gauze.

At a point in the wound in the anterior abdominal wall at its most prominent part (see Figure IV), which was at about the junction of its upper and middle thirds, a circular aperture, large enough to accommodate three fingers or more, was made by cutting out a portion on either side, comprising all its layers. Through this aperture the sigmoid colon was led in such a way that it formed a gentle curve downwards and forwards from the pelvic brim. The abdominal wound was then closed in layers around this colostomy. The colon was then divided at a point which would leave a stump of about two and a half inches projecting externally. The colostomy was then attached by means of a Paul's tube to a large-bore rubber drainage tube, which was allowed to drain into a bottle. The wound was sealed with "Nobectutane", an impervious, transparent, non-irritating material.

The object of this technique, apart from removing the cancer and viscera described, was, firstly, to construct a "wet" colostomy in such a manner that there would be no sphincters, no obstruction and no sump formation in the colon—nothing in fact which would interfere with the free flow of urine. By avoiding the factor of obstruction it was hoped to minimize the effects of possible infection in the renal tract. The second object was to construct a "wet" colostomy stoma in such a manner that after healing it would project from the anterior abdominal wall in the form of a spout, and so allow the continuous dribble of urine to pass directly into a rubber colostomy bag and not pass over the skin (see Figure V). In this way it was hoped to avoid excoriation and infection of the skin surrounding the colostomy.

During the operation difficulty was experienced in freeing the pelvic portions of the ureters and overlying peritoneum from the lateral walls of the pelvis, owing to dense fibrosis resulting from the previous operation. A pint or so of blood was lost in a matter of seconds when a cruciate type of anastomosis between four large veins was opened while we were laying bare and dissecting amongst the branches of the sacral plexus on the right side. At the time when the structures in the pelvic floor were being divided, prior to the removal of the mass of viscera and for a few minutes thereafter, the patient was pulseless and the sphygmomanometer failed to register. The occurrence of severe shock at this stage is not unusual during the course of an operation of this magnitude. During the closure of the abdominal wound and the fashioning of the colostomy her condition rapidly improved, so that at the completion of the operation the pulse rate was 100 per minute and the systolic blood pressure had risen to 120 millimetres of mercury. An hour or so later the patient was placed on her bed in the theatre and returned to the ward.

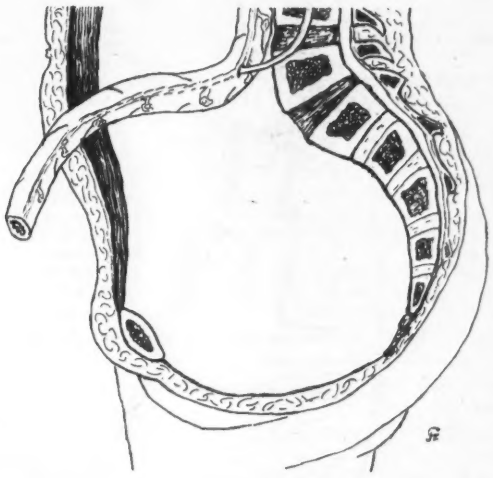

FIGURE IV.
Uretero-colic anastomosis at the pelvic brim. "Wet" colostomy in the mid-line below the umbilicus.

The mass of viscera was sectioned in the mid-sagittal plane. The growth was found to occupy the space between the bladder and the rectum, as already indicated (see Figure I). It was about the size of a small walnut, and bilobular in shape, with the left portion already ulcerating through the trigone of the bladder (see Figure II). It formed a projection posteriorly, which extended into the lumen of the rectum, without as yet invading its walls. On microscopic examination carcinoma cells were found in small groups scattered throughout the tumour.

Continuous gastric suction was instituted and intravenous infusion maintained. Urine was noticed passing through the colostomy within a few hours of the operation, and within twelve hours some eight ounces had been passed. For the first four days after operation, after daily estimations had been made of the blood urea and serum biochemical constituents, the fluid and electrolyte balance was maintained by continuous intravenous infusion of fluid containing the appropriate electrolytes.

Within forty-eight hours, with the patient under "Pentothal" anæsthesia, the gauze pack was removed from the pelvis and the perineal wound closed by mass interrupted sutures of nylon, a space being left posteriorly occupied by a rubber drainage tube. This was gradually shortened and finally removed after five days. Although the temperature remained elevated between 100° and 102° F., and the pulse rate ranged between 100 and 120 per minute, for the first six days, the abdomen did not show any distension, nor did the patient's general condition give any cause for

alarm. Penicillin and streptomycin were given during the period of pyrexia, together with a liberal amount of vitamins, which were given parenterally during the early stages.

The colostomy continued to drain satisfactorily through the Paul's tube for six days; then, after loosening had occurred, it was removed.

A "Davol" rubber colostomy bag was then fitted (see Figure V), and its surface of contact was sealed to the skin surrounding the colostomy by an adhesive, non-irritating, rubberized solution of the same name. The

FIGURE V.

"Wet" colostomy with rubber bag attached and the junction sealed with "Danol" rubberized solution.

patient was ambulant from the sixth post-operative day. On November 23 the colostomy was trimmed, and on November 29 the patient was discharged from hospital.

To date, some eight months after operation, she has remained well and, to use her own words, has "not had a temperature, an ache or pain since leaving hospital". She has returned to her normal life, does her own housework, drives her car and plays bowls. The management of the "wet" colostomy has caused her no trouble. The colostomy bag is emptied as required, without being detached from the abdominal wall. A rubber band is removed from the aperture at its lower end, and the contents, which are always fluid, are allowed to pass into the lavatory. The bags, of which she has two, are changed and cleaned every second day. There have been no leaks. There is no smell. The skin surrounding the colostomy has remained normal. She now wears for comfort a specially designed corset, and under her ample, flowing and pleated dress any bulge caused by the bag is completely hidden.

Discussion.

A total of 441 exenteration operations for advanced pelvic cancer have now been performed by Alexander Brunschwig and his associates (personal communication, April 7, 1956). Originally the objective aimed at was palliation only. It has been found, however, that of the patients with cancer in stage IV previously considered inoperable and unsuitable for any form of active treatment, 12% of the first 104 have survived for more than five years. Of the 89 patients operated on during the period 1950-1951, 28% have remained alive without evidence of the disease for three years.

Although completely unselected with regard to age and general physical condition, the only selection being that the disease should appear to be confined to the pelvis, of the first 315 patients operated on 17·7% died within thirty days of operation. A further 8·8% died after this period, but without leaving hospital, which gives a total mortality rate for this operation of 26·6%.

Early diagnosis and treatment of cancer undoubtedly offer the best chance of permanent cure. The opportunity of successful palliation and even cure in late cases which is offered by surgery should not be lost sight of. No longer need the patients in late stages be abandoned. The suggestion that these patients should be allowed to die in peace is the outcome of a mentality of defeatism. It is not borne out by the facts, for it is well known by those who are accustomed to deal with them that these patients do not die in peace.

It is reassuring to know that certain of the larger medical centres in this country are sufficiently well staffed and equipped to deal successfully with these cases.

Summary.

A case of total pelvic exenteration for recurrent carcinoma of the cervix is described and used to illustrate the following points:

1. The opportunity of salvage in advanced cases of cancer.

2. The minimum of inconvenience afforded by modern appliances to the patient with a wet colostomy.

3. The availability of this procedure in our larger teaching hospitals.

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Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Drugs and Doses of the British Pharmacopœia 1953 and the Addendum 1955 with Therapeutic Notes and Indicating Related Preparations of the Australian Pharmaceutical Formulary 1955"; 1956. Melbourne: The Council of the Pharmaceutical Society of Victoria. 7" × 4¼", pp. 97.

Designed to give assistance to Australian medical practitioners prescribing under the National Health Service.

"Ciba Foundation Symposium, Jointly with The Physiological Society and The British Pharmacological Society, on Histamine, in Honour of Sir Henry Dale, O.M., G.B.E., M.D., F.R.C.P., F.R.S." Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc.; 1956. London: J. and A. Churchill, Limited. 5¼" × 8", pp. 488, with illustrations. Price: 50s.

One of the Ciba Foundation Symposia recording papers read and discussions by international authorities.

The Medical Journal of Australia

SATURDAY, JUNE 23, 1956.

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A SPECIAL UNIT FOR CANCER RESEARCH IN NEW SOUTH WALES.

SOME eyebrows were raised and shoulders were shrugged at the announcement last year that the Government of New South Wales had decided to establish a New South Wales Cancer Council. Those who indulged in these expressions of surprise or of non-concern probably thought of similar ventures which in the public mind had not justified their establishment, or doubted the sincerity of a Government harassed by disturbances and activities lightly dismissed as merely political. How would such a government, they asked, be able to pay serious attention to the problems presented by such a condition as cancer? Had not the best brains in the world failed to explain cancerous growth? Perhaps this was merely political eyewash to do something for cancer patients. And so on. It is always wrong to prejudge a question. Of course, one might ask if it would matter whether political eyewash was being used provided patients suffering from cancer were helped and their unfortunate lot was ameliorated. And who will dare to say that Australian investigators working on the cancer problem are unlikely to shed light on one of its dark corners? Any efforts that the New South Wales Government, or any other Government or body, makes should be welcomed and if possible piloted along right channels, or shall we say promising channels, which may lead to some further useful point of departure, if not to the wished-for harbour. Our object at present is to explain what the New South Wales State Council is intended to do, to lay stress on one of its truly admirable features and to plead for the cooperation of the members of the medical profession to make it effective.

The *New South Wales State Cancer Council Act*, 1955, to use its "short title", was assented to on April 26, 1955. The objects for which the Council was established are set out as follows:

(a) to assist and foster research and investigation with respect to the causation, prevention, diagnosis and treatment of cancer;
(b) to assist and foster post-graduate and undergraduate education and training, and education of the public, with respect to cancer;
(c) to assist in providing training and instruction in technical matters relating to the diagnosis and treatment of cancer;
(d) to co-ordinate, so far as is practicable, the activities of all institutions, hospitals and other bodies engaged in research and investigation with respect to the causation, prevention, diagnosis and treatment of cancer;
(e) to conduct public appeals for funds for carrying out the above objects;
(f) in consultation with the Hospitals Commission of New South Wales, to advise the Minister on problems relating to—
  (i) the provision of hospital accommodation for the treatment of persons suffering from cancer;
  (ii) the provision of facilities for research and investigation with respect to the causation, prevention, diagnosis and treatment of cancer;
  (iii) the establishment of a cancer institute;
(g) to advise the Minister on such other matters relating to cancer as the Minister may from time to time require;
(h) to initiate and refer to the Minister recommendations on any matter relating to cancer.

The objects of the Act are most comprehensive and the new Council has ample powers, for it "may do and perform all acts and things that are necessary or convenient for giving effect to the objects" set out above. The following are members of the Council: Emeritus Professor S. H. Roberts, Vice-Chancellor of the University of Sydney (chairman); Dr. A. B. Lilley, Chairman of the Hospitals Commission of New South Wales (deputy chairman); the Honourable R. R. Downing, Attorney-General, Minister for Justice and Vice-President of the Executive Council; Dr. B. T. Edye; Professor E. Ford; Sir Edward Hallstrom; and Mr. J. Shortell, President of the Trades and Labour Council.

We have no wish to discuss the activities of this new Council in relation to other bodies controlling or endowing research in the Commonwealth. It may be useful, however, to point out that the proposed coordination to be fostered between all other bodies is to be only "so far as is practicable". Our intention is to discuss the responsibility of the Council regarding "the provision of facilities for research and investigation with respect to the causation, prevention, diagnosis and treatment of cancer". This is to be done "in consultation with the Hospitals Commission of New South Wales". The Commission made available thirty beds for the purposes of cancer research at the Prince of Wales Hospital, Randwick, when that hospital was taken over by the Board of Directors of Sydney Hospital. These beds were the basis of the new research unit. In July, 1955, the Cancer Council approached Dr. Kenneth W. Starr, a member of the honorary medical staff of Sydney Hospital, and invited him to become honorary director, that he might "create, organize and direct" the new unit. Before he accepted the offer Dr. Starr laid down as a condition of his acceptance certain desiderata to which the Council agreed. These were: (i) Treatment must rank equally with investigation. (ii)

Intermediate and public accommodation must be provided for men, women and children. (iii) The unit must be self-contained and independent of other scientific, clinical and operative hospital facilities. (iv) Extensive scientific facilities are imperative on the highest international scale of staff, equipment and records. (v) Medical and nursing staff must be of sufficient seniority to enable them to understand the scientific and clinical undertakings in which they are engaged. The objects and limitations of the special unit must be emphasized. It is not intended in any way to supplant the therapeutic facilities of the great hospitals; as a matter of fact the unit will not be equipped to do this. What is intended is that certain lesions shall be studied exhaustively from the metabolic and biological points of view. It is consequently of importance to have patients suffering from these lesions—all of them may not be frankly cancerous. Clearly the small number of beds cannot be used to accommodate patients dying of cancer nor those in desperate plight when all types of treatment have failed to give relief. In order to obtain the appropriate lesions for intensive study, the special unit will carry out treatment by surgery and combine this with chemotherapy and radiotherapy; in this use will be made of the facilities of the Sydney Hospital. It is estimated that patients will be admitted in July, 1956, when structural alterations being made are completed. Accommodation is being provided for public and intermediate patients, both adults and children. Patients will be admitted to the unit through the beds of the Prince of Wales Hospital, Randwick; applications for admission should therefore be addressed to the Medical Superintendent. Members of the profession will be kept notified through the pages of this journal of the various lesions which are under study in the hope that appropriate patients will be selected by their medical attendants and directed to the unit.

The Government of New South Wales is to be congratulated on setting up this special unit and particularly on having agreed to the conditions imposed by Dr. Starr. The provision of all that will be needed in the way of staff, equipment and the keeping of records is much to be commended and will surely be the envy of others less fortunately placed. The success of the unit will be judged by its clinical achievements, but of much greater importance will be the facts gained from the intensive study of lesions. All these will be woven, with those acquired from many other sources, into what we regard as the exceedingly complex pattern of malignant disease until in the fullness of time the whole is made clear. It is not too much to ask for the cooperation of the practising members of the profession to make this new venture successful.

Current Comment.

BLADDER "SUBSTITUTES".

REMARKABLE imagination and ingenuity have been displayed by surgeons in their attempts to devise a substitute for the urinary bladder and to incorporate it satisfactorily into the urinary excretory system. For a reservoir various parts of the bowel have been used, and surgical techniques in great variety have been developed, but mostly incorporating basic ideas tried out half a century ago, more or less, according to John J. Murphy.[1] In 1895 implantation of the ureters into the rectum after proximal sigmoid colostomy was described, and in a subsequent modification the isolated rectum was anastomosed to the urethra. Somewhat different was the use of an isolated segment of ileum as a urinary conduit to the intact sigmoid colon. Verhorgen in 1908 implanted the ureters into the isolated caecum and used the appendix to convey the urine to an opening on the abdominal wall. In 1911 an operation was described in which a segment of ileum was isolated, its proximal end was closed, and (after implantation of the ureters) the distal end was brought through the anal sphincter. Murphy quotes the statement of Hinman that these were "nothing more than elaborate devices for urinary stagnation", but goes on to point out that attempts to find a satisfactory reservoir for urine, of the types described, have continued.

Early efforts to prevent peritonitis and urinary fistulæ after uretero-enterostomy led to the development of a variety of techniques of ureteral implantation. These have been modified, discarded, revived and again modified, and so on; but the ideal has not yet been achieved. Methods have included: various "tunnelling" techniques; extraperitoneal implantation of the ureters; implantation of the "intact ureter" into the bowel wall without entering the bowel lumen while the ureter was still in continuity with the bladder, the uretero-enteral fistula being created later by a variety of "aseptic" techniques; transplantation of the intact ureteral orifices from the bladder wall to the bowel; various "flap" techniques to prevent transmission of pressure and infection from the reservoir to the upper part of the urinary tract; open transcolonic anastomosis of the ureters to the sigmoid colon as it overlies the sacrum.

Murphy states that careful evaluation of results obtained with the many modifications of reservoir and implantation techniques has provided clarification of many problems, but solution of few. He lists three main factors affecting the function of "bladder substitutes". The first is obstruction, which may occur at the site of ureteral transplantation or at the outlet of reservoir or conduit, or may be the result of intraluminal pressure of reservoir or conduit. The second is infection; this may come from the exterior by means of tubes, catheters and the like, or from the interior of the conduit or reservoir. The third is absorption of urinary constituents, which has been shown to play a part in the pathogenesis of the electrolyte imbalance so frequently noted after uretero-enterostomy; it is dependent upon the surface area, the absorbing powers and the intraluminal pressure of the conduit or reservoir. These, Murphy points out, are the problems which must be solved to make "bladder substitutes" physiologically feasible. That they may not be impossible of solution is indicated by the fact that an occasional patient with uretero-sigmoidostomy gets along quite well clinically and maintains apparently normal renal function and pyelographic appearance for many years. The solution appears to be in creation of a valve at the ureter-"bladder" junction to protect the kidneys from back pressure, ureteral reflux and ascending infection. The only other solution with any promise is the physiological conduction of the urine to an external appliance, the idea of an internal reservoir being abandoned. Cutaneous ureterostomy, one of the oldest methods, has been revived, but has many disadvantages. More promising has been the development of a technique in which an isolated segment of bowel is used purely as a conduit of urine. A reliable leak-proof adherent bag provides the reservoir function. Clinical experience to date has emphasized the renal protection offered by this method, as well as its reasonable "social convenience".

In his case report on total pelvic exenteration in the treatment of recurrent cancer of the cervix published in this issue, J. Cameron Loxton describes the successful use of the method reported by A. Brunschwig and V. K. Pierce[2] in 1951. Brunschwig and Pierce's paper is not mentioned in Murphy's review of the subject, but it

[1] *Am. J. M. Sc.*, February, 1956.
[2] *Arch Surg.*, January, 1951.

appears to have considerable merit. It consists essentially of implantation of the ureters into the lower part of the sigmoid colon and the establishment of a "wet" colostomy. Brunschwig and Pierce expressed themselves as satisfied with the method in 1951 after using it in over 100 cases, and Brunschwig and William Daniel[1] were still employing the method in 1954. In quite extensive experience they had not found infection or hyperchloræmic acidosis a major problem. They write: "The incidence of pyelitis or other later complications has never been such as to raise, at any time during the past 7 years, the question of the compatibility of the operations with indefinite survival." Loxton's report, although only of a single case, is well in accord with this experience.

GASTRIC HÆMORRHAGE AND ACUTE INTRACRANIAL VASCULAR ACCIDENTS.

IN 1952 J. D. French and co-workers began the report of a clinical and experimental study of gastro-intestinal hæmorrhage and ulceration associated with intracranial lesions with the statement that gastro-intestinal complications in patients with intracranial lesions were so common that they should be recognized whenever they occurred.[2] They discussed 17 cases in which gastro-intestinal hæmorrhage or hæmorrhagic erosion was associated with intracranial disease. It is of interest, too, that in 1953 R. J. Hoxsey reported five cases of acute bulbar poliomyelitis associated with gastric hæmorrhage.[3] It will be remembered that the late Harvey Cushing had a practical interest in this subject. In 1932 he wrote at the start of an article on peptic ulcers and the interbrain[4] that his interest in the subject had been incited by the disturbing experience of having lost three patients from acute perforations of the upper part of the alimentary canal soon after what appeared to be successful operations for removal of intracranial tumours. Interest in this subject, which does not appear to be recognized by clinicians as it should be, has been stimulated by a valuable article from A. Doig and J. Shafar.[5] They write from the Burnley Group of Hospitals, Lancashire. They describe seven cases of gastric hæmorrhage, each of which occurred in association with a spontaneous intracranial hæmorrhage. Only one of the patients recovered. In every case there was clinical evidence of bleeding in the alimentary tract; in the seventh case blood was found in the stomach at autopsy. The first case was one of subarachnoid hæmorrhage and hæmatemesis was the presenting feature. No macroscopic lesion was found in the alimentary tract, but small areas of mucosal damage were found in the stomach. The second case was one of cerebral hæmorrhage in which hæmatemesis occurred one and a half hours after the onset of illness. Numerous petechial hæmorrhages and ecchymoses were found in the gastric mucosa. In the third case, one of subarachnoid hæmorrhage and transient hyperglycæmia, hæmatemesis occurred eight hours after the onset of coma; recovery followed. The fourth case was one of cerebral hæmorrhage and hæmatemesis occurred shortly after the onset of the illness. At autopsy a small quantity of blood was found in the stomach; the entire gastric mucosa was congested and many punctate hæmorrhages and small hæmorrhagic erosions were present. In the fifth case, one of pontine hæmorrhage, hæmatemesis occurred one hour after the onset. At autopsy the internal surface of the stomach was covered with mucus which contained a mixture of fresh and altered blood, the gastric mucosa was congested and a large number of punctate hæmorrhages were present in the proximal two-thirds. The sixth case was one of cerebral hæmorrhage and occult blood was found in the fæces twenty hours after the onset. At autopsy the stomach contained some altered blood; in the proximal part of the organ there were in the mucosa many superficial erosions, punctate hæmorrhages and ecchymoses. In the seventh case, one of cerebral hæmorrhage, gastric hæmorrhage was found at autopsy and the gastric mucosa was extensively involved with petechial hæmorrhages and ecchymoses. The brief statement on Doig and Shafar's cases will serve to show the kind of thing that happens. They are typical of many others which will be found scattered through the literature. Doig and Shafar state that hæmatemesis and melæna have been reported in the following conditions: intracranial neoplasms, meningitis, head injury, bulbar poliomyelitis, intracranial hæmorrhage of the newborn, cerebral infarction, intracranial aneurysm, encephalitis, choreoathetosis, cerebellar cyst, and as a sequence to frontal lobotomy and pneumoencephalography. When we look at this formidable list with the names of many authors mentioned under each heading, we cannot think that the concurrence is fortuitous. This view is expressed in spite of the opinion of some authors that there is no ætiological relationship between the conditions. Doig and Shafar state these opinions with great frankness. For example, they refer to an analysis of 2437 autopsies performed at Zurich in 1947 and 1948; here Betz found the combination of intracranial lesions and chronic peptic ulcer to be no greater than the calculated chance association. If, then, we agree that there is a causal connexion, we must ask why more gastric complications of intracranial lesions are not reported. If they exist but are not noticed, then Doig and Shafar's paper becomes all the more welcome. In any case our immediate concern should be with the mechanism by which the gastric lesion is brought about.

The first thing to be noted is that these mucosal hæmorrhages, erosions or ulcers found in association with intracranial disease differ in no way from those found in patients who have no intracranial disease or from those produced in animals by experimental means. The hæmorrhages are usually situated superficially in the mucosa; when they are well formed they are wedge-shaped or cone-shaped, the base being on the free surface of the mucosa. Sometimes, though not so often, hæmorrhages occur in the deeper layers of the mucosa and then they are irregular in shape. Doig and Shafar consider the vascular anatomy of the gastric mucosa and base their statements on a study by Barlow, Bentley and Walder,[1] a study which is readily available to most practitioners. After reference to this and to the work of other authors, they point out that the cause of most of the erosions was superficial mucosal hæmorrhage and not the less frequent deep mucosal hæmorrhage. In most instances the erosions were funnel-shaped and on a few occasions a vertical mucosal vein in the base of the lesion was closed by a thrombus. "The fact that no venous thrombi were seen unless an erosion was present is strong presumptive evidence that the thrombosis is not primary but probably secondary to the exposure of the vessel to the gastric juice." At that rate we must discover what it is that brings about exposure of the vessel; in other words we must discover the cause of the primary vascular disturbance in the mucosa. This is far from simple. Doig and Shafar write that the accepted theory that the acute gastro-intestinal lesions associated with intracranial disease are due primarily to vascular disturbances in the mucosa is strongly supported by the histological findings in their cases. They add that the cause of the local vascular disturbance has been disputed. Thus one observer held that the primary disorder was dilatation and stasis of the blood vessels consequent on vasomotor paralysis. Others looked on prolonged vasoconstriction as the essential underlying factor. According to a third view the vascular disturbance is due to compression of arteries and veins by spasmodic contractions of the gastric musculature. What is stated to be another possible mechanism is that introduced by the recent demonstration in the human stomach of arterio-venous anastomoses in the submucosa, capable of short-circuiting the mucosal arteries directly into the veins. Venous dilatation and perivascular hæmorrhages were observed in all Doig and Shafar's

[1] *Surg., Gynec. & Obst.*, 1954, 99: 324.
[2] *Surg., Gynec. & Obst.*, 1952, 32: 395.
[3] *Arch. Int. Med.*, 1953, 92: 662.
[4] *Surg., Gynec. & Obst.*, 1932, 55: 1.
[5] *Quart. J. Med.*, January, 1956.

[1] *Surg., Gynec. & Obst.*, 1951, 93: 657.

specimens; this, they state, is characteristic of partial or complete stasis.

All this does not offer a solution of the main problem. Something happens in the cranium which has an action, seemingly specific, on the gastric mucosa. If a vasomotor action is set up, we must know why. It is justifiable to ask whether a biochemical agent is responsible. Doig and Shafar refer to work that has been done on the secretion of corticotrophin, and to action of the hypothalamus, as well as to the effect of operations on the plasma levels of 17-hydroxycorticosteroids. And we may well ask why selective action on the stomach takes place. Apparently the stomach, which in some ways is more tolerant of insults than any other organ of the body, is specially sensitive to certain occult biochemical or neurogenic influences. Examples of the latter have been supplied by French and his co-workers who produced hæmorrhages in the gastro-intestinal tract of animals on whom they had previously inflicted a hypothalamic injury.

TO SEE OURSELVES AS OTHERS SEE US.

FOR many members of the medical profession it would be salutary if they could discover what opinions were held about them and their work by those among whom they practised. Some people may be disdainful of public opinion, but the doctor is foolish to adopt this attitude. Sick people as a rule consult the man whom they like; because they like him they are the readier to accept what he tells them and to do his bidding in the matter of treatment. Some medical men with brusque manners and even with rude and offensive ways seem to build up professional reputations which line their purses and no doubt flatter their vanity. The truth probably is that their reprehensible qualities pass as a sign of what is known as "cleverness": "Yes! but he's so clever, you know." But it is not only "clever" people of this kind who should be given a chance to benefit from learning the truth about themselves. (The "clever" folk, of course, might not, probably would not, benefit.) The opportunity should be as widespread as possible.

The American Medical Association has been thinking along those lines and has done something about it. It employed an independent research organization to conduct a public opinion poll. Personal interviews were conducted in Chicago with 3000 members of the general public, 500 medical graduates in private practice and 100 persons in each of the special groups—editors, columnists and commentators, lawyers, pharmacists, registered nurses and executive secretaries of State and County medical societies.[1] The 3000 members of the general public were asked questions about general public attitudes; the professional groups were asked largely about professional and organizational matters. The present communication deals only with the views of the general public. The information from the professional groups will be published later on in three or four instalments. That the American Medical Association was very much in earnest is shown by the fact that 289 "professional surveyors" were engaged in the work. The financial cost must have been fairly large.

It may be useful in this instance to state the general conclusion at the outset because it agrees with what is currently believed in this country. "People's attitudes toward their own doctors are based upon their own personal experiences, while their attitudes toward doctors in general must necessarily be based upon secondary information and hearsay." In all parts of Australia most people look on their own doctors as reliable and reputable, but many of them become unreasonable and wickedly malevolent when they refer to the "B.M.A.". Unfortunately they are often encouraged in this attitude by some notoriety-seeking newspapers whose editors publish misstatements about the Association and refuse to correct them. But let us return to Chicago. It was found that large percentages of the general public claimed to have a family or personal physician. About five out of six or 82% of the general public made this claim. Farm dwellers reported the highest percentages of family doctors (90%) and non-whites the lowest (73%). Few persons who changed family doctors did so because of personality clashes or loss of respect. Most of the changes of doctors were made because they moved, or because the doctor moved or entered military service, or because the doctor became ill, retired or died. Only 5% reported that they had lost confidence in their doctor, 2% had found "a better doctor", and 1% disagreed with the doctor's diagnosis or treatment. Of the five special professions surveyed all but the druggists thought as highly as, or even more highly than, did the general public. The number of druggists who said that they liked their own doctors as persons was 5% less than the average for other groups. Some questions were worded in such a way that those interviewed replied "true" or "false". The following is one tabulation:

	My Doctor. True.	Most Doctors. True.
Do you think:		
Doctors think they are better than most people?	5%	25%
Doctors have the idea that they are always right? ..	23%	43%
Doctors keep people with appointments waiting longer than necessary?	15%	41%
Doctors are hard to reach for emergency calls?	19%	51%
Doctors are slow to try new drugs and treatments? ..	7%	11%
Doctors are too quick to recommend an operation?	5%	31%
Doctors are not as dedicated to serving mankind as they should be?	6%	27%
Doctors plan to get rich quick?	10%	30%
Doctors charge too much? ..	16%	53%
Doctors' charges have gone up faster than other living costs?	13%	35%

One of the questions asked was: "What do you like about most doctors?" The reply from 30% was "friendly, personality, manner"; 19% replied: "personal interest, sympathy, kindness"; 18% replied: "competent, intelligent, educated"; 13% replied: "heal you, cure you"; 13% replied: "sincere, dedicated, try to help"; 10% replied: "frank, honest". Other replies from groups of less than 10% are set out in eight groups; some 11% replied that they did not know.

The general conclusion to be drawn from this report of the American Medical Association's investigation is the great value of the family doctor. It may be said that we have known this all along. That is true, but it is also true that if you can measure something you know more about it. The figures are admittedly American, but for all that they have a certain application to our own medical set-up. The analysis of the replies from the professional groups will be awaited with interest, though possibly they may not be so applicable to Australian conditions as are those from the general public.

[1] *J. Indiana M. A.*, March, 1956.

TREATMENT OF CARDIAC ARREST.

SUDDEN cessation of cardiac function in the absence of heart disease occurs occasionally in the operating theatre. The patient is usually young and was previously quite healthy and had shown no signs of intolerance to the procedure of anæsthesia. There is no means of detecting patients in whom the syndrome of cardiac arrest is likely to occur and death is the almost invariable outcome unless very vigorous measures are instituted without delay. Even when the circulation is reestablished the delay may already have resulted in irreversible changes in vital centres so that a mere physiological heart-lung preparation is established, the death of the individual has already taken place

and the death of the body is soon inevitable. Besides the terrible tragedy of cardiac arrest under anæsthesia, similar episodes occur which are due to reflex vagal inhibition, with drug intoxication (especially digitalis glycocides), and as a characteristic of specific diseases with a resultant Stokes-Adams syndrome. In many cases because of delayed recognition and treatment of the condition the actual cause of death is of little more than academic interest. The time during which the body can afford to dispense with its oxygen supply is so short that treatment can be envisaged only when the cardiac arrest occurs when the patient is under close medical supervision. The standard methods of treatment devised for patients outside the operating theatre involve the intracardiac administration of cardiac stimulating drugs. Under suitable conditions cardiac massage with or without thoracotomy has been used to some considerable extent. On the whole the results have been very disappointing and only a small number of patients survive either owing to or in spite of these procedures. From the Harvard Medical School have come several reports of the use of an externally applied cardiac pacemaker which stimulates the heart electrically. The instrument thus devised is portable and maintains an externally placed ventricular rhythm for as long as is necessary.

P. M. Zoll, A. J. Linenthal, L. R. Norman, M. H. Paul and W. Gibson[1] have described the use of this instrument in the cardiac arrest of the Stokes-Adams syndrome. This syndrome follows the familiar pattern of cerebral ischæmia owing to profound ventricular slowing, ventricular standstill or ventricular fibrillation occurring as a result of atrio-ventricular heart block. In all, 27 patients with profound slowing or cessation of ventricular action have been rapidly resuscitated and some were resuscitated many times. In no patient was the ventricular rhythm restored when it was impaired by tachycardia or by fibrillation. Continued stimulation was sometimes necessary for several days before a spontaneously acceptable rhythm was reestablished. Of the patients, ten survived for at least one month and seven for over a year. Eighteen patients died because no machine was available in a subsequent episode of cardiac arrest. From their results the authors conclude that the use of the electric pacemaker is the treatment of choice in the Stokes-Adams syndrome, though drug therapy is used to help in withdrawing the machine. It was also found that the pacemaker was equally effective in the repeated resuscitation of three patients with reflex vagal cardiac inhibition. The treatment was equally effective for cardiac arrest due to digitalis, procainamide and quinidine.

In a more recent paper Zoll *et alii*[2] describe the use of the external pacemaker in the unexpected cardiac arrest which occurs during surgical procedures. The rate of recovery after emergency thoracotomy is low and the other less formidable procedures, while safer, are even less effective. Eight successful electrical pacemaker resuscitations after cardiac arrest are reported. In none were thoracotomy and cardiac massage necessary. Five patients recovered completely, two died of unsuccessful cardiac surgery, and one died several hours after the operation. In seven other cases in which the stimulation was applied five minutes or more after arrest, and in two in which the arrest was due to ventricular fibrillation, the treatment was ineffective. The authors suggest that in view of the crucially short interval of time before cardiac arrest is irreversible, a practical monitoring device capable of signalling the cessation of cardiac pulsation could be cheaply applied as a routine device during anæsthesia preferably by means of electrocardiographic methods with an audible alarm for the cessation of activity. Precautions against anæsthetic explosion are necessary in this kind of procedure. Staff should be familiar with resuscitation and it should be applied without delay. The electrical pacemaker should be applied at once unless it is known that the fault is one of ventricular fibrillation. Intracardiac needle puncture and epinephrine hydrochloride injection may also be performed while the pacemaker is being applied. Ideally the instrument can be applied as a routine measure before the operation with the electrodes five to eight centimetres apart on the precordium. If the pacemaker is ineffective after one minute of stimulation thoracotomy should be performed. The authors state that defibrillation by electrical shock or by drugs may be followed by cardiac arrest for which the electric pacemaker would be effective. After resuscitation, they hold that the pacemaker should be attached ready for immediate use for the first two or three days, as the cardiac arrest frequently recurs.

[1] *J.A.M.A.*, December 10, 1955.
[2] *New England J. Med.*, March 22, 1956.

CŒLIAC DISEASE AND HEREDITY.

It has been known for some years that cœliac disease may occasionally be found in the near relatives of affected children. The exact pattern and the frequency of the hereditary factor have not been calculated. More recently it has also appeared likely that the typical form of cœliac disease may be only the most severe manifestation of a genetic character tending towards a wide variety of gastro-intestinal disturbances.

P. H. Boyer and D. H. Andersen[1] have made a careful study of the genetic role of cœliac disease and also of the association of this disease with *diabetes mellitus*. The pedigrees of 50 children between the ages of six months and five years, each diagnosed as suffering from cœliac disease, were carefully studied. In each instance the diagnosis was made on clinical and laboratory criteria at the Babies' Hospital, New York. Half the children provided typical examples of the most severe forms of the disease and the rest suffered from a milder type with starch intolerance. In each case fœtal fat starch determinations were made by microscopic examination of the stools. The family pedigrees of 50 control children were also closely studied for evidence of gastro-intestinal disturbances of a constitutional nature. Parents were interviewed separately to avoid the shielding of familial inadequacies. Cases were carefully selected so that the relatives were already well known and most likely to cooperate. For the same reason the control children were those of the hospital staff.

In the study of the families of cœliac children it was found that there was a particular tendency to recurrent unexplained episodes of diarrhœa or loose stools, sometimes precipitated by emotional factors, particularly in the parents of the child, and often referred to as "nervous stomach". Many appeared to have an unduly active gastro-colic reflex and diarrhœa was often associated with the ingestion of cow's milk. Several relatives had fat and fried food intolerance of the gall-bladder dysfunction type and there were histories of food allergy or even of well-established cœliac disease. Of these cœliac children, there was cœliac disease in 23·7% of the siblings, in 5% of the parents and in 1·1% of the siblings of the parents. No cases occurred in the families of the control group. There was no significant difference in the familial incidences of peptic ulcer, gall-bladder disease and allergic conditions. Of the 50 cœliac families there was a diabetic family history in 27, and in 14 of these two or more persons were found to be suffering from *diabetes mellitus*. Of the 50 control families there was a diabetic family history in 15, and in seven of these, two or more persons had *diabetes mellitus*. From these figures it would appear that cœliac disease is associated with a familial tendency to *diabetes mellitus*. However, when possible errors in comparing the two groups are taken into account, the difference is not statistically of significance and the authors conclude that cœliac disease and *diabetes mellitus* are probably not associated in the same genetical pattern. Moreover, the incidence of cœliac disease and other unexplained gastro-intestinal disturbances was significantly higher in the relatives of cœliac children. The exact nature of the gene concerned remains to be discovered, though the associated and hereditary nature of cœliac diseases and several non-specific gastro-intestinal disturbances is confirmed.

[1] *J. Dis. Childhood*, February, 1956.

Abstracts from Medical Literature.

RADIOLOGY.

The Lower Œsophageal Ring.

R. SCHATZKI AND J. E. GARY (*Am. J. Roentgenol.*, February, 1956) describe a thin diaphragm-like constriction known as the lower œsophageal ring which is not infrequently found if the lower end of the œsophagus is distended with a barium mixture. The œsophagus may appear to be completely normal unless it is sufficiently distended. Occasionally this diaphragm is still clearly visible in the collapsed œsophagus. This narrowing represents a thin annular portion of the wall of the œsophagus which cannot be distended as well as the wall both above and below this region. The maximal diameter of the ring is usually constant for several years. The ring occurs with equal frequency in males and females. It is considerably more common in persons past the age of fifty years. The ring must be differentiated from simple muscular contraction of the œsophagus and from hiatus hernia with or without œsophagitis. The cause of the ring is unknown. The ring is frequently associated with a hiatus hernia, and it appears likely that some upward displacement of the intestinal tube into the chest is present in all patients in whom the ring is demonstrated. In most instances the ring produces no clinical symptoms; in a smaller group of persons it results in dysphagia with characteristic sporadic episodes of difficulty in swallowing solid food. Fortunately the treatment is considerably less problematical than the nature of the ring. Since it appears that the patient will have dysphagia only if there is a discrepancy between the known size of the ring and the size, and to a certain degree the consistency, of the bolus which he swallows, it is necessary to inform the patient of the nature of his lesion. He should understand the necessity of eating slowly and of decreasing the size of the bolus.

Respiratory Distress in the Newborn.

R. E. STEINER (*Brit. J. Radiol.*, September, 1955) discusses the importance of radiological studies of infants suffering from respiratory distress. The radiographic appearances in the various respiratory troubles of infancy are described and an attempt is made to differentiate the radiological signs of primary pulmonary collapse, pneumonia and hyaline membrane. In the case of primary atelectasis, if this is total, both lungs, as might be expected, are opaque and no air will be detected in the trachea or major bronchi; the child is stillborn. In most cases, however, primary atelectasis affects only one lung or segment of lung, in which case only that particular segment appears opaque on the radiograph. Secondary signs of atelectasis may be present, such as rib retraction or associated mediastinal shift. The unaffected lung appears well expanded and normal. Primary lobular atelectasis is rare, in which case the pulmonary pattern of the affected area is rather mottled, but the distribution of the opacities is, on the whole, of a segmental nature. Primary atelectasis can clear very rapidly within hours, but the reverse process can occur so that a small collapsed segment of lung progresses to total collapse. Pneumonia is a complication which may develop within a few hours of birth, and in the few instances where a diagnosis can be made radiologically, the appearances are those of bronchopneumonia rather than lobar consolidation. Pneumonia is often a complicating factor of primary atelectasis and hyaline membrane; under these conditions an accurate diagnosis is very difficult indeed. In fact, the appearances of bronchopneumonia, with its rather coarse, diffuse pulmonary mottling and the later stages of hyaline membranes may be indistinguishable. Hyaline membrane is common in premature babies but less so in full-term infants. There are a number of stages in the development of this condition. The earliest radiological sign which appears within a few hours of birth is a fine, miliary mottling of fairly uniform distribution clearly visible in both lung fields. Under treatment this mottling can clear within hours or days, leaving a perfectly normal lung, and this clearance coincides with the clinical improvement of the child. If the disease process is progressive, the mottling changes from a fine miliary pattern to a coarse one within hours or days; eventually confluent areas appear which may involve one lobe or the whole lung and finally there is total consolidation and collapse. It appears, therefore, that hyaline membrane either may lead to complete pulmonary collapse with subsequent death, or it may clear and the child recover completely.

Cranial Manifestations of Familial Metaphyseal Dysplasia.

P. A. MORI AND J. F. HOLT (*Radiology*, March, 1956) state that characteristic cranial changes may accompany familial metaphyseal dysplasia or Pyle's disease. The principal features are diffuse symmetrical hyperostosis of the skull and mandible, with associated hypertelorism and obliteration of the paranasal sinuses. Encroachment on neural foramina may produce cranial nerve deficiencies. The diagnosis of familial metaphyseal dysplasia is dependent upon the radiological observation of splayed long bones. When typical hyperostosis of the skull is present in conjunction with splayed long bones the diagnosis can be established by röntgenograms alone. Several other conditions in which this feature may occur must be differentiated. Symmetrical splaying of long bones may be caused by (i) bone marrow hyperplasia, (ii) bone marrow infiltration, (iii) deficiency states, (iv) developmental abnormalities, and (v) toxic substances. In the bone marrow hyperplasia group are included erythroblastic anæmia and, rarely, sickle-cell anæmia and chronic hæmolytic icterus. When bone marrow hyperplasia is sufficient to produce a splayed appearance of the long bones, widening of the diploë in the skull and swollen contours of the metacarpals and phalanges may be expected. These findings permit the radiological recognition of the bone marrow hyperplasias. In the bone marrow infiltration group are Gaucher's disease and the leuchæmias. In the early form of Gaucher's disease the radiological appearance of the long bones is virtually identical with that in familial metaphyseal dysplasia. In such cases differentiation is dependent upon the clinical and pathological observations. In more advanced cases destructive lesions are present in long bones. The same is true of leuchæmia. Such lesions are not seen in familial metaphyseal dysplasia. The deficiency states producing splayed long bones include fibrocystic disease of the pancreas, healing scurvy, and healing rickets. Clinical and pulmonary findings aid in the recognition of fibrocystic disease. Healing scurvy and healing rickets usually are sufficiently characteristic in themselves for a diagnosis. A moderate degree of cranial hyperostosis may be present in healing rickets. The developmental diseases in which splayed long bones may be observed include osteopetrosis, gargoylism and cleidocranial dysostosis. In osteopetrosis there is dense sclerosis of the cranial base and to a lesser degree of the vault. Differentiation is made by the diffuse sclerosis of the ends of the long bones, a feature not found in familial metaphyseal dysplasia. Hyperostosis of the skull and splayed long bones may on very rare occasions be seen in gargoylism. Other features of this condition provide a basis for differentiation.

Luschka Joints of the Cervical Part of the Spine.

A. G. BOREADIS AND J. GERSHON-COHEN (*Radiology*, February, 1956) have reviewed the anatomical aspects of Luschka joints in the lower cervical part of the spine and have correlated these aspects with the röntgenographic appearance. Lyschka joints are small synovial articulations, measuring from two by four to three by six millimetres, and situated between the five lower cervical vertebral bodies. They are located antero-medially to the mixed nerve root and postero-medially to the vertebral artery vein and sympathetic nerves as these all pass through the vertebral foramen. The Luschka joints participate with the intervertebral disc and vertebral body in the formation of the anterior wall of the foramen. Upon separation of the vertebral bodies there may be observed, upon the upper surfaces of their postero-lateral aspects, convex spur-like ridges, consisting of spongy bone and covered by cartilage. On the corresponding undersurface of the vertebral body are concave areas, also covered by cartilage. These two structures come into apposition and are covered by synovial membrane to form the Luschka joints. As true synovial joints, they are subject to the diseases common to such joints. Their proximity to nerve roots, vessels, ligaments and discs results in early manifestation of disease, even when the synovial membrane only is involved, without röntgenographic evidence of bone or joint irregularities. In later stages of arthritis, fibrous adhesions and demonstrable spurring may cause marked and unremitting symptom-

atology because of pressure on the adjacent vascular and nerve structures. It is suggested that greater röntgenographic attention to disease of these joints would contribute toward elucidation of the shoulder-hand syndrome, and hence aid in the differential diagnosis of this syndrome from peritendinitis of the shoulder joint.

PHYSICAL THERAPY.

Radiation Hazard Evaluation and Control in Hospitals.

G. FERLAZZO, T. NICHOLSON, A. JACOBSON AND M. BUSHMAN (*Radiology*, December, 1955) point out that the scope of radiological protection encompasses all practicable, convenient and economical procedures for rendering the medical applications of ionizing radiations reasonably safe for all patients and personnel concerned and for the public at large. The principles and practice of radiological protection have been evolved since the discovery of radium, and nothing essentially new has followed the introduction either of artificial radioactive isotopes or of very high voltage apparatus. The scope of the work in this field of the medical physicist is discussed. The increasing use of radioactive isotopes is accompanied by an increase in the number of inexperienced personnel in the field and in the consequent possibility of undue exposure. The authors conclude, however, that radium and radon and X rays in fluoroscopy are still the major sources of external radiation hazards in hospitals. By comparison, the external hazard for radioactive isotopes is minimal, with the exception of C^{60} and of G^{198}, used instead of radium or radon. The internal hazards from the medical use of radioactive isotopes also seem to be minimal if the medical physicist is familiar with their handling and gains the cooperation of all concerned. All radiation hazards can be minimized and kept well within permissible limits without unduly elaborate facilities. Planning and training are important.

Appraisal of Radioactive Iodine Therapy.

A. L. SCHULTZ AND L. ZIEVE (*Am. J. Med.*, January, 1956) suggest that after the use of radioactive iodine in the treatment of hyperthyroidism the evaluation of response to therapy is often made difficult by the delay in the regression of clinical symptoms and signs. A reliable means of predicting the failure of therapy within the first few weeks after treatment would be of great practical value. In an attempt to evaluate the effects of treatment, the authors have studied the changes in the tracer studies following treatment by radioactive iodine. Sixty-six hyperthyroid patients, each of whom received therapeutic doses of radioiodine, were according to the results assessed after treatment into three groups comprising respectively failure, remission, or resulting myxœdema. Studies were made of the clinical status of the patient, the rate of thyroid uptake, the basal metabolic rate and determinations of the serum cholesterol content and protein-bound iodine content. It was evident when studies of these three groups were made that there was in each an overall difference prior to treatment. Hyperthyroidism had been previously more marked in those patients who tended to fail with radioactive iodine. The determination of the basal metabolic rate was the only test differentiating significantly all three groups for treatment. Within six to nine weeks after treatment the patients who responded were clearly distinguishable by the thyroid uptake. The basal metabolic rate showed a similar change, but the estimations of serum cholesterol were somewhat less effective in differentiating failures from remissions. From the study of a limited number of patients the estimations of protein-bound iodine appeared to be at least as effective as studies of the basal metabolic rate in differentiating the responses of the patients to treatment. Almost all those patients who had shown the clinical signs of hyperthyroidism and whose thyroid uptake and basal metabolic rate were both either abnormally high or borderline at their first adequate post-therapy evaluation, proved manifest eventual treatment failures. The rate of failure was not quite so high among those patients who were found to give one or more normal responses to tests early in the convalescence. As early as six to nine weeks, over one-half of the patients in the remission and myxœdema groups, but only one-twentieth of those in the failure group, had non-palpable glands. At later intervals the authors found that the group differences were even more striking.

Time Dose Studies in the Radiation of Mycosis Fungoides.

M. FRIEDMAN AND A. W. PEARLMAN (*Radiology*, March, 1956) state that a construction of iso-effect recovery curves for each type of tumour is a necessary step towards improvement of the knowledge of radiation dosage. It is suspected, though not demonstrated, that different types of tissue have specific recovery rates. *Mycosis fungoides* is a useful test object for study of the recovery rate, because the multiplicity of lesions permits confirmation of each given dose by means of the corroborated dose technique which the authors describe in the paper. In the treatment of two patients with a large number of lesions a useful iso-effect curve was constructed for each. Furthermore, it became possible to compare the iso-effect curve of a markedly radiosensitive tumour with that of one which was only moderately radio-sensitive. The corroborated dose technique previously employed by the authors in the study of recurrent skin nodules of breast cancer was used in this case to obtain iso-effect curves based on the minimum tumour lethal dose. After irradiation, the lesions were observed for a period of four to six months. Treatment was considered to be successful if there were no recurrences during this period. The two patients were irradiated with different doses in different overall time periods, according to the corroborated dose technique. An iso-effect curve was constructed for each patient and the two curves were compared with each other and with curves previously published. A mathematical recovery or fractionation factor was derived for each curve but was not entirely valid, since the paucity of points permitted several types of curves to be fitted to each group of points. The resulting curves proved to be useful guides for the clinical radiation therapy of *mycosis fungoides*. The radiosensitivity classification of any tumour is usefully symbolized in terms of the corroborated minimum lethal tumour dose for a single exposure. In the two cases reported, the dose was 250*r* and 800*r* respectively. This compares with the skin cancer dosage of 2200*r* and that for recurrent breast cancer of 2000*r*. The authors state, however, that this does not imply that the lesions of *mycosis fungoides* are treated preferably by a single dose of irradiation.

Radiothorium (Th^{228}) in Radium Poisoning.

M. A. VAN DILLA AND B. J. STOVER (*Radiology*, March, 1956) report on the work that has been done in a long term study on the chronic toxicity of plutonium deposited in the skeleton. Since man could not be used as an experimental subject, the work has been done with the dog, an animal whose skeletal system approximates to that of the human. There exists already a considerable body of knowledge on chronic radium poisoning in man. What has been called radium poisoning has frequently involved poisoning by mesothorium (Ra^{224}) and radiothorium (Th^{228}). These radioactive materials are the only two long-lived daughters of the thorium series. Like radium, they are deposited chiefly in bone. Although these radio elements emit α, β and γ rays, the α radiation is the most damaging of these to tissue. In calculations of the total α energy delivered to bone it is essential to know whether the daughter products stay put or wander elsewhere in the body. In the experiments, Th^{228} in radioactive equilibrium with its daughters was injected by the intravenous route. By the method used 80% to 90% of the injected Th^{228} was quickly deposited in the skeleton and remained there for the first six to nine months after injection. It was found that this stability was not a characteristic of the daughter products. About 40% of Ra^{224} produced in the Th^{228} decay was excreted and failed to irradiate the skeleton. The daughter product of Ra^{224} is thoron, an inert radioactive gas which is an isotope of radon. Measurements show that 10% to 15% of the thoron produced leaves its site of formation in bone, roughly half of it decays in the blood, while the other half is exhaled. It is apparent that while the Th^{228} is tightly bound to bone, the amount of its daughters escaping is such that 61% of the α energy produced actually irradiates the bone. It was also clear that Th^{228} delivers over twice the α energy to bone that results from equal activity of radium or plutonium. Hence it might be expected that Th^{228} would be more toxic than either radium or plutonium in the first six to nine months after injection.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on April 26, 1955, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. E. F. THOMSON, the President, in the chair.

Reserpine and Chlorpromazine in Medicine and Psychiatry.

DR. D. R. MORGAN read a paper entitled "The Use of Reserpine, Chlorpromazine and Allied Drugs in Medicine and Psychiatry" (see page 1029).

DR. E. T. HILLIARD read a paper entitled "The Use of Reserpine, Chlorpromazine and Allied Drugs in Medicine and Psychiatry" (see page 1035).

DR. F. HALES WILSON, in opening the discussion, said that it seemed to him that a new chapter in the treatment of mental illness had been opened, which was certain to lead to a much greater understanding of the inner mechanisms of mental derangement and of normal mental processes. As in many other fields of medicine, the biochemists would be the ones to solve the problems ultimately. Dr. Wilson thought that those present should be grateful to the psychiatrists for what they had told them. Those who were practising general medicine badly needed the advice of the psychiatrists as to the limitations and indications of the use of the drugs under discussion. Physicians were also anxious to know how long the treatment should continue, what the ultimate relapse rate was going to be and what the long-term effects might be. When new drugs were introduced, there were always a number of unsuspected things which they were able to do which were not found out for some years, and no doubt that would be so with the drugs being discussed. If they continued to have their present success, then more and more patients would be out of hospital and taking them, so that it would become more and more important that clinicians should know about their effects, and in the case of chlorpromazine about its action on sensitivity to morphine *et cetera*. As Dr. Hilliard had mentioned, the new treatment would raise a tremendous rehabilitation problem. Dr. Hilliard had also said that the old methods of treatment, which now seemed to have been very peculiar, at least gave a recovery rate of 30%. Dr. Hales Wilson said that he had been much interested in that remark; he wondered whether anyone could really tell with certainty what was the recovery rate of the untreated disease. He thought it highly probable, though he spoke subject to correction by the experts, that 30% was the recovery rate of the untreated disease. Dr. Hales Wilson then referred to the medical applications of the substances in general medicine. He said that physicians had found reserpine most useful in the treatment of hypertension in many cases. Its action was unpredictable; sometimes it had an excellent effect, and sometimes it had none. That was not surprising, since in the vast majority of cases of hypertension the mechanism and cause were unknown. There again the application of that drug would probably lead to a greater understanding and a more detailed classification of the causes of hypertension and a greater knowledge of the underlying mechanism. Certainly in most cases in which hypertension needed to be treated, he had found that reserpine was the best drug to begin with. Dr. Hales Wilson agreed with Dr. Swanton that reserpine was not a drug to give to patients not under supervision, because in some cases its side effects, especially its depressive side effects, would be harmful. His inclination then was to stop the drug, rather than to supply another potent weapon to neutralize undesirable side effects. In cases in which it was not sufficiently effective, it combined very well with ganglion-blocking agents such as pentolinium. Dr. Hales Wilson said that he himself had had only limited experience in the general medical use of chlorpromazine; he acknowledged its enormous application in psychiatric practice. He thought that it had not a great application in general medicine. There was a great tendency at the present time to give the patient chlorpromazine when one did not know what to give him or what to do for him. That was an unfortunate and undesirable attitude to medical treatment. From what he had read in the literature, Dr. Hales Wilson did not at all regard it as a harmless drug. Apparently it had behaved well in the experience of Dr. Morgan and Dr. Hilliard; but at least one case of aplastic anæmia had been reported. Dr. Hales Wilson was sure that for one reported there were certainly many others that had been recognized and not reported and some which had not even been recognized. He could not help regarding any phenothiazine derivative as a potent and potentially dangerous drug which should not be used without a very clear indication. He freely acknowledged that the indications were very clear in psychiatric practice; but the drugs should not be generally given to all kinds of people in ordinary medical practice. With regard to the occasional occurrence of jaundice, Dr. Hales Wilson said that he could not explain its cause. It seemed to have the characteristics of retention jaundice, and therefore it might lead to difficulty in the case of older patients. One would not know whether the patient had a neoplasm causing obstructive jaundice, or whether the jaundice was due to chlorpromazine. Most of the patients seemed to have recovered, but sometimes rather slowly, over a period as long as three months, and he had noticed only one death reported in the literature, apparently due to toxic diffuse hepatitis. The knowledge that jaundice could occur should make physicians very careful to inquire in any case of jaundice whether the patient had been taking chlorpromazine; otherwise an unnecessary laparotomy might be undertaken to seek the cause of obstructive jaundice.

DR. G. L. EWAN said that he had been interested in both papers, and particularly in Dr. Hilliard's recapitulation of treatment used in the early days, as he had been a contemporary of Dr. Hilliard's and had passed through the whole gamut of treatments mentioned. Schizophrenia was, of course, known to be a very malignant type of psychosis, and in the old days they had very little at hand to relieve the patient. When thyroid medication together with the exhibition of parathyroid was introduced, and the drugs were "pushed" until a good physiological response was obtained, many psychiatrists thought that at last something had been introduced which would be a panacea for that illness. They did obtain some remarkable results, which it was now realized were in many cases due to spontaneous remissions, known to occur in that disease. Possibly in those times there was a closer interpersonal relationship between the psychiatrist and the patient. In the present mechanized times the treatments in hospitals were more scientific, and with the shortages of staff perhaps the patients did not receive the psychotherapy that was so essential. Dr. Hilliard had mentioned the financial aspect of the use of the drugs under discussion. Dr. Ewan said that he himself was an officer responsible for authorizing the use of the drugs, and from the administrative point of view it was necessary to satisfy the laymen concerned with the budget that the tremendous expenditure involved was justified. The drugs were extremely expensive and were now being exploited throughout the State mental hospitals; the amount of money involved ran into thousands of pounds per month. Dr. Ewan said that he was not so much concerned with the number of recoveries as with the number of patients who were granted leave. Even if only one patient was granted leave from the mental hospitals for twelve months, the amount of money expended on the drugs for the treatment of such a patient as an out-patient was readily offset. In addition Dr. Hilliard had pointed out that the drugs provided a great deal of comfort and help for those patients who had to remain permanently in institutions. Another important factor was the great relief they afforded to the nursing staffs in institutions. Also there was no doubt that the drugs had brought about some very spectacular results. However, it was necessary to take care not to attribute all the spectacular results to the drugs. Other factors were involved; one was the general attitude of the staffs to the new treatment and their enthusiasm; and there were other psychological imponderables that had to be taken into account. Dr. Ewan wondered whether at Parramatta any control series had been used with their patients. In the literature from the United States, some of the psychiatrists had carried out carefully controlled experiments with the drugs. Only recently he had seen the results reported from one hospital where they had used a large series of controls. Some patients were treated with chlorpromazine, and the officers treating them did not know which subjects were receiving placebos or drugs, and which subjects were controls. Very favourable results were obtained in both groups. After the experiment was over the subjects in both groups were examined by psychiatrists, psychologists and physicians, in an attempt to determine which subjects had received the treatment. It turned out that 58% of the subjects were correctly detected as having received the drug. Dr. Ewan said that care was necessary in testing and in avoiding bias; control series should be used. He did not know of any experiments of that nature having been carried out in the State institutions up to the present. Dr. Ewan finally asked whether the clinicians had noticed any effect of the

drugs along the lines of cloaking or masking symptoms due to some intercurrent disease or infection, so that the diagnosis might be missed.

DR. S. BENEDEK referred to the importance of the subject under discussion. He said that those psychiatrists who were in private practice were being persecuted, because it seemed that all the good results went to the Mental Hospitals Department. However, not only private psychiatrists but also some American workers had apparently not always had good results. He had seen a report of many cases of agranulocytosis following the exhibition of the drugs, and in his own practice jaundice had occurred in three cases. He believed that the drugs were excellent in institutions. However, their only use was in the treatment of disturbed psychotic patients, and if the psychiatrists did not curb their enthusiasm, sooner or later every patient with any kind of psychiatric disorder would receive chlorpromazine.

PROFESSOR W. S. DAWSON said that he had very limited experience of the drugs in the more florid type of psychosis, in which apparently they had a remarkable effect. How long-continued that effect would be remained to be seen, and also how long patients would be able to tolerate the exhibition of the drugs. In the psychoneuroses when the drugs were given to ambulant patients, he thought that the results on the whole—perhaps more particularly those following treatment with chlorpromazine than with "Serpasil"—were far less predictable and far less satisfactory, except perhaps in cases of anxiety with a considerable degree of tension. It seemed that the more intense the symptoms, the greater the degree of tension or anxiety or aggressiveness, on the whole the more satisfactory were the results. But outside mental hospitals, in spite of occasional benefits, it appeared that they were still faced with the problem of various ways of dealing not very successfully with the chronic neurotic. Particularly in those cases in which the patient had obsessive ideas, if there was no intense emotion attached to those ideas, to that extent they were less responsive to the newer remedies.

DR. O. SCHMALZBACH had a question to ask. He said that recently in looking up the literature on the subject of chlorpromazine, he had found in a review from New York covering the last twelve months an incidence of more than 14% of hypochromic anæmia. Dr. Schmalzbach wondered whether Dr. Morgan and Dr. Hilliard had encountered such a complication. Dr. Schmalzbach further said that some years previously when he was on the staff at Broughton Hall under Dr. Guy Lawrance, "Serpasil" had been tried in about 100 cases of psychoneurosis of various types. They had not reached the dosage levels reported from Parramatta Mental Hospital; however, the results were so disappointing that the treatment was abandoned after a trial of a few weeks.

DR. SELWYN NELSON said that from the general medical point of view he thought that chlorpromazine had some value, even though one had not the courage to use it in the doses in which it could be used when the patient was under close supervision in a mental hospital. Dr. Nelson said that he was referring particularly to cases on the borderline between the psychiatric and the medical, which could be classified possibly as psychogenic rheumatism. In such cases the patient had a disturbed psychological background manifesting itself as tension, in particular of the muscles. In such cases, even in doses of 75 milligrammes a day, chlorpromazine did give a satisfactory result in a sufficiently high proportion of cases to justify its use. The method of control was to compare the patient receiving treatment with the patient when treatment was discontinued. It seemed to him that the treatment had been proved to be a continued maintenance treatment rather than a short-term curative treatment. Dr. Nelson said that he had been impressed by the careful presentation of the papers and the astonishing results achieved; he was sure that they were better than the natural history of the diseases. As far as "Serpasil" or reserpine was concerned, it was used in medicine extensively as a hypotensive drug. One learned to fear it in certain cases as a producer rather than an alleviator of mental illness. There were cases in which retention of fluid and sodium seemed to occur, which made continuation of the treatment undesirable, and in other cases the side effects that were noticeable on the higher doses were also noticeable on the lower doses. The sedative effect of reserpine did not seem to be very noticeable in general medical practice, and the effect on the blood pressure was that most desired. One had to avoid hastening to use the new remedy while it yet cured; but he thought that carefully controlled observations such as those presented by Dr. Morgan and Dr. Hilliard would show that, unless some long-term disadvantage was discovered, the use of the drugs opened up a new era in psychiatric medicine.

DR. JAMES ISBISTER said that he had been gratified to hear of the good results achieved in psychiatric practice, and of the pharmacological basis for them. As a general physician he used very little chlorpromazine; he believed he could truthfully say that he had seen more cases of side effects from it than cases in which he had given it himself. He had seen eight patients with jaundice from chlorpromazine in the general medical wards. Dr. Isbister quoted the case of a woman who had a varicose ulcer of the leg, and was given an ointment to apply which produced a sensitivity reaction. She was then given cortisone to treat the sensitivity reaction, and that made her mentally rather odd, so she was given "Largactil". She was then taken to hospital with jaundice, her varicose ulcer being well and truly healed. As Dr. Wilson had said, very often chlorpromazine in particular was given by people other than psychiatrists as a last resort in a rather complicated problem, or when other forms of therapy had produced ill effects. Dr. Isbister felt that just as surgery was better carried out by a surgeon, so chlorpromazine and similar drugs might be better left in the hands of the psychiatrists, at least for the time being, until more was known about them. In that regard Dr. Isbister asked what the psychiatrists thought about the almost routine use of chlorpromazine by obstetricians for the treatment of vomiting of pregnancy. It seemed to him to be an undesirable thing to do. He had had no personal experience of it.

DR. HELEN TAYLOR said that she had been interested in Dr. Morgan's statement that reserpine had produced not bradycardia but tachycardia. In treating patients with hypertension she had found bradycardia to be the rule.

DR. G. L. HOWE said that as a general practitioner he had come to the meeting to learn what he could about the use of the drugs. The late Sir Archibald Collins used frequently to say that one should not use a drug until one knew all about its use. Dr. Howe said that he had learnt a lot about the use of chlorpromazine and similar drugs in psychiatry, and he was astounded at the huge doses used. He was interested in Dr. Isbister's question; he himself had even given chlorpromazine in morning sickness in very small doses (10 to 25 milligrammes), and the results were extraordinary. In some cases it was very successful, some patients had been asleep nearly all day, and in some cases it had had no effect whatever, as might have been expected from the exceptionally small doses. In view of what had been said at the meeting, it seemed to him that what was needed was a pharmacologist *plus* a physician with knowledge and experience of the drug to tell them what was its use in general practice. Dr. Howe said that he had been impressed with the figures given in relation to the treatment of the severely mentally ill; but as for its other uses, he did not think much had been learnt at the meeting.

DR. W. H. FRASER asked the speakers to comment on the use of chlorpromazine for the relief of pain in inoperable cancer; he said that some of his surgical friends were enthusiastic about it.

DR. H. R. BAILEY spoke on the subject of leucotomy in relation to chlorpromazine; he said that to him its future appeared very poor indeed, and it would certainly be replaced by more precise stereotaxic techniques. He did not think that it would survive for many more years in its present form. Dr. Bailey went on to refer to the general status of the drugs under discussion in American and European medicine. He said that, going through a large number of American mental hospitals, he had formed the impression that they could be divided into two groups—those that were chlorpromazine conscious and those that had somewhat more reticent views about it. Dr. Bailey commented on the figures that had been given earlier from the Manhattan State Hospital, where chlorpromazine was used almost as a routine drug on a patient's admission to hospital, to such an extent that some hundredweights of the drug were used per month. Dr. H. C. Denber, whom Dr. Bailey knew well, was completely converted to the use of the drug for all patients admitted to a mental hospital. It was the feeling amongst some workers in the United States, including Dr. Harold Himwich, that chlorpromazine and similar drugs were being grossly overused, and were entering on the second phase of the use of all new drugs, when the swing was slightly to the left after all the difficulties and scepticism following their introduction. In those hospitals where carefully controlled studies had been carried out to determine the effects of the drugs in long-standing psychoses, it had been found that many more factors were concerned than appeared on the surface affecting the response of the patient to moderate doses of the drug. A great deal of work was going on in that regard, particularly in Sweden, where large-scale investigations were being carried out in

mental hospitals on the problem of the variables concerned. Referring finally to the question of dosage, Dr. Bailey said that responsible workers now felt that when one had to give doses up to the order of four or five grammes of chlorpromazine per day (which, of course, had been given by those people), that was rather ridiculous. In the majority of cases control was satisfactory on doses of the order of 300 to 500 milligrammes.

Dr. Morgan, in reply to Dr. Hales Wilson, who had inquired about jaundice, said that in almost all cases in which jaundice had been reported in the literature—and there had been a number of deaths from obstructive jaundice—small doses of the drug had been used. A small dose might be defined as about 25 milligrammes perhaps twice or three times a day. It was very rare for jaundice to occur in cases in which the initial dosage was 100 milligrammes twice a day. It seemed that there might be some sensitivity reaction connected with the formation of obstructive jaundice. It was difficult to be dogmatic on the subject, because many much more experienced workers overseas were still not of one mind on the matter. Dr. Benedek had raised the question whether the drugs should be used only in institutions. Dr. Morgan said that he thought chlorpromazine had some use outside when its use had become more widely known among general practitioners. It was possible that such use of the drugs might keep out of the mental hospitals many patients who now had to be admitted to them, and permit them to be treated as out-patients. Dr. Morgan felt that if there was a clinic in Sydney where psychiatric patients could be treated on a walk-in, walk-out basis, it would be likely to save a large number of admissions to hospital, which were very costly. Professor Dawson had referred to the use of the drugs in the psychoneuroses. Dr. Morgan said that the Americans had a new drug, "Miltown", which they called the "DOL't give a damn" pills, because the tense, emotional person who was full of repressed aggression could take that drug, which was allied to mephenesin. Two Los Angeles drug stores had sold a quarter of a million tablets in the four months during which the general public had been able to obtain it. Dr. Morgan said that it had a great vogue, and he did not doubt that when it came to Australia it would have a great vogue here also. It relieved tension, perhaps far more than reserpine did. In reply to Dr. Schmalzbach's question on anæmia, Dr. Morgan said that he had not seen it occur. In reply to Dr. Isbister, who had asked about the vomiting of pregnancy, Dr. Morgan said that it was true that chlorpromazine could be used. He knew a man who had recently been abroad and had taken "Largactil" as a preventive of seasickness; probably as good or better results would have been obtained with "Avomine", another phenothiazine derivative, which was directed against vomiting. In reply to Dr. Nelson, Dr. Morgan said that chlorpromazine had quite a field of application in anæsthesia, but he had no experience of it. Dr. Taylor had reported the occurrence of bradycardia with chlorpromazine treatment, whereas at Parramatta tachycardia had been the rule; Dr. Morgan said that he could only quote their own examples. He thought that out of all the patients in the series, he had seen two with bradycardia. It was not severe enough to require cessation of administration of the drug; the pulse was slow, but that was not a side effect found to be distressing. In the main, when the blood pressure had been rapidly lowered, especially in elderly hypertensives, almost invariably tachycardia occurred.

Dr. Hilliard, in reply to Dr. Hales Wilson, who had asked about the recovery rate of the untreated disease compared with the 30% of recoveries obtained by old forms of treatment, said that he was unable to answer the question. Possibly the early forms of treatment were of the same nature as the treatment of pneumonia—directed towards keeping up the patient's strength and preventing him from exhausting himself. Dr. Ewan had asked whether placebos had been given; Dr. Hilliard said they had been mixed with the drugs, although the medical officers had known when placebos had been used. That was not exactly what Dr. Ewan required. However, placebos had been used in order that patients should not rely entirely on the drugs. They had been given to some patients on leave. Dr. Benedek seemed to think that they waited until patients became psychotic and then got the mental hospitals to cure them. It was posible, as Dr. Morgan had said, that agranulocytosis occurred with the smaller doses. Professor Dawson's question about the results of long-continued dosage could not yet be answered. The longer one waited, the more accurate the results would be. Dr. Schmalzbach had mentioned the occurrence of hypochromic anæmia, before they had received any treatment with chlorpromazine. Dr. Hilliard wondered whether Dr. Schmalzbach's patients were examined before treatment or after. The patients were examined frequently during the course of treatment, and showed no significant difference. In reply to Dr. Taylor, Dr. Hilliard said that there was one point that could have been mentioned in the papers, the use of reserpine in the treatment of hypertension. The physicians knew that it was so used. But if the patient had hypotension or a blood pressure normal for the age group, reserpine did not reduce the blood pressure. Dr. Hilliard said that he could not discuss the use of chlorpromazine in obstetrics, except to say that when it had been given in small doses of 25 milligrammes it had had exactly the results mentioned; some patients were improved, others became ill, and still others developed a rash or other strange symptoms. Dr. Hilliard regretted that no one had answered Dr. Fraser's question about the use of the drugs for the relief of pain. He said that was the original use of chlorpromazine, for which it was sought and discovered. Since the drug did relieve tension and also pain, it was necessary to watch the patient's health carefully. Dr. Hilliard believed that the drug could mask the early symptoms of illness. That was a factor that needed to be taken into account particularly in private practice. Dr. Hilliard had been interested in Dr. Bailey's remarks about the use of chlorpromazine in all admissions to the Manhattan State Hospital, and also about the large doses. Dr. Hilliard agreed with Dr. Bailey that it was not necessary to give doses up to such heights.

Dr. Thomson, from the chair, thanked Dr. Morgan and Dr. Hilliard for their informative papers, which deserved high commendation, and referred to a point made by Dr. Ewan on the question of finance. He said that to him it seemed a terrible thing that when the public utility of health came into the picture, the Treasury officials immediately clamped down on the money. He thought it high time that the medical profession took an interest in the fact that the finance of the public utility of health seemed secondary to the finance of other public utilities. The proposed further 10% cut in the expenditure of hospitals was completely impossible, and the profession should take a stand about it.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

GOVERNMENT AND GENERAL ORDERS.[1]

Government House,
Sydney,
12 July, 1817.

CIVIL DEPARTMENT.

WHEREAS several Abuses have arisen from the irregular and unwarrantable practice of Settlers and Overseers employed for Landed Proprietors residing in the Interior having taken upon themselves to grant Passes to their Assigned Servants to come to Sydney or to go to other Places at a Distance from their Service: and whereas other Evils and Injurious Consequences have arisen from there not being a regular Mode of Communication or Report heretofore from the Surgeons of the Government Hospitals where any such Assigned Servants are received as Patients not only as to the time when they were received but also the Periods when they were discharged therefrom, thereby affording them an Opportunity instead of returning to their Masters Employ to wander about the Country and to betake themselves to idle and profligate Courses, to the injury of their Masters and the Public at large. It is therefore hereby ordered and directed with a view to prevent the Recurrence of Such Abuses. . . .

The Surgeons of the different Hospitals on receiving a Male Patient (being a Government Assigned Servant) are required to take down the Name of such Patient and the Name and Residence of his Master: and on the Discharge or Death of such Patient to report the Circumstance forthwith to the Magistrate of the District from whence the Patient had been sent: and to furnish such servant when discharged from the Hospital with a pass to return direct to his Master's Service.

By Command of His Excellency the Governor,

J. T. CAMPBELL, Secretary.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

AN ACCIDENT WITH A ZIPPER.

SIR: Concerning the problem of zipper flies on wearing apparel, the following case may be of interest.

A young man, in some haste, caught his prepuce firmly between the two plates of the glider of the zipper. Being the down-stroke, he was thus prevented from completing the opening "slide". At the same time, if he had pulled the glider up, his skin would surely have been caught in the closed teeth of the zipper.

In this dilemma he sought medical advice and was treated as follows. The whole zipper was removed from the trousers, the lower locked end was then broken with a pair of ordinary pliers and the zipper teeth freed up to the impacted glider. Each lateral runner was then gripped above and below the glider and wrenched from it. The two plates of the glider could then be easily separated and the whole withdrawn. There was only a minimum of abrasion and bruising.

Yours, etc.,

128 River Road, Revesby, May 20, 1956. B. W. COOMBES.

THE TRENDS OF MEDICAL PRACTICE.

SIR: Our fellow practitioners in England, according to the *British Medical Journal*, are finding the position difficult. They say that £3700 a year is now only equal in purchasing power to £800 a year before the last World War. The sum of £3700 a year is apparently a specialist's remuneration under the English health Act—and the ordinary practitioner on apparently 50% to 70% of that finds himself working on an overdraft and unable to get ahead.

Of course, it is easy to say that such an unfortunate position is the natural result of medicine becoming practically a State department, and some will call it socialism, which it certainly is not. England is not a socialist country, and the trend to what is better termed "Statism" is matched in all non-socialist countries. For example, in the United States of America, the leader of such countries, the Government now buys 25% of the goods and service produced annually and has seven and a quarter million civil servants. (One worker in every eight is a civil servant.)

In Australia we, too, have to face a rapidly increasing cost of living, behind which our fees are lagging considerably. Also, whether we like it or not, the State is making increasing inroads and the sphere of the traditional private practice is becoming smaller and smaller.

Is it not time that we investigate the causes of these redoubtable trends, and establish a prognosis, that is, find out where we are going?

Perhaps we might change our largely passive attitude and endeavour to play some part in determining our own fate.

Are we taking part in progress or reaction? Whose interests are being served by this hypertrophy of the State? Have our Council or our members any information on these subjects?

Yours, etc.,

473 Bourke Street, Melbourne, May 24, 1956. G. P. O'DAY.

MOLLUSCUM SEBACEUM, SELF-HEALING EPITHELIOMA AND TUMOUR-LIKE KERATOSIS.

SIR: I have been extremely gratified to note the interest that the above-named paper (M. J. AUSTRALIA, April 28, 1956) has raised, both in dermatological and surgical circles. Mr. Hueston's letter (M. J. AUSTRALIA, May 19, 1956) has raised some very interesting points as to the endemiology of *molluscum sebaceum*.

Mr. Hueston, in Melbourne, notes four out of his fifteen cases of *molluscum sebaceum* to involve the hands, while Beare (1953), in describing 76 cases seen in Belfast, did not find one involving the hands or fingers. A similar experience to Beare was noted in all the reports available up to the latter half of 1955, when I wrote the above-named paper. Added to that is the fact that, in several hundreds of cases of squamous-cell carcinoma involving the hands, this is the first case I have seen that clinically and microscopically was established as *molluscum sebaceum*. We are thus presented with an interesting problem of endemiology or geographical pathology.

The second feature that I stressed, that of more than one lesion of *molluscum sebaceum* occurring in the same individual, is also regarded as not worth the mention by Mr. Hueston. I did not, however, notice any references in Mr. Hueston's letter as to the other authors who have reported such occurrences. That multiplicity of lesions might be expected on a theoretical basis is, of course, undoubted, but all authors in the literature of this disease, which now comprises several hundred cases, stress the solitary nature of *molluscum sebaceum* as a distinguishing characteristic from the multiple types of Poth, of Ferguson Smith and of Witten and Zak. To try and establish the link between these entities was my reason for writing this paper.

It would appear, therefore, that my suggested lack of familiarity with the appearance of *molluscum sebaceum* in the hand and its multiple occurrence is shared by every authority who had written on the subject before my paper was conceived. Mr. Hueston, in his letter, suggests that the criteria of MacCormac and Scarff in the diagnosis of *molluscum sebaceum* are now out-dated, and has possibly established his own personal criteria. This might account for the unusual endemiology of the cases he described.

Yours, etc.,

Peter MacCallum Clinic, 483 Little Lonsdale Street, Melbourne. May 24, 1956. BASIL A. STOLL.

HERPES ZOSTER OPHTHALMICUS.

SIR: The circular to members of the New South Wales Branch of the British Medical Association dated May 21, 1956, contains a notice indicating that the Director-General of Health in Canberra, A.C.T., has made γ globulin available for the treatment of *herpes zoster ophthalmicus*.

Could the Director-General or his advisers elaborate on this form of therapy, explaining the rationale and giving, if possible, references to the literature? As far as I can ascertain, only brief and scant mention is made of γ globulin in the treatment of *herpes zoster ophthalmicus* and that it may be of some benefit in relieving pain.

Finally it is my opinion that any such treatment should be carried out by an ophthalmologist under whose care all patients suffering from *herpes zoster ophthalmicus* should be. *Herpes zoster ophthalmicus* is a most serious ocular disease with many dangerous complications, and statements such as those which appear in the circular may give a general practitioner a false sense of security, although no such intention existed.

Yours, etc.,

9 Butler's Road, Hurstville, May 22, 1956. R. HERTZBERG.

THE FEE FOR MAKING AN AUTOPSY.

SIR: Under the heading "Out of the Past" published some months ago in THE MEDICAL JOURNAL OF AUSTRALIA there was an extract from the *New South Wales Government Gazette* of the year 1818, stating the fee for making a post-mortem examination was two guineas (£2 2s.).

The fee for government medical officers making a post-mortem examination is still £2 2s., and for giving evidence in the coroner's court £1 1s. This is hard to realize, but is a fact. The fee for giving evidence in the higher court is now £3 3s. for attendance each day and £1 1s. for evidence.

When one considers the time occupied, the inconveniences associated with interviews with the police, and the writing of reports, the remuneration is obviously absurdly inadequate.

Whose duty is it to have this anomaly corrected? It is hardly the province of any individual country government medical officer.

Yours, etc.,
"G.M.O."

Sydney,
May 28, 1956.

AUSTRALIA AND DIPHTHERIA IMMUNIZATION.

SIR: The *Chronicle of the World Health Organisation* gives the following table in Volume 10, number 3, page 83, March, 1956:

TABLE I.

Country.	Proportion (*per Centum*) of Deaths from Diphtheria in Relation to General Mortality (All Causes), 1951 to 1953.	
	Children Under Ten Years Old.	Children Four Years Old.
Australia	0·6	3·4
Canada	0·1	0·8
Finland	0·2	1·7
France	0·2	1·2
Italy	1·2	7·5
Netherlands	1·7	9·7
New Zealand	0·1	1·8
Norway	0·1	1·0
United Kingdom ..	0·1	0·8
United States of America	0·1	0·9

Australia ranks so high among those countries often used for comparisons that it is of interest to give a detailed table of the deaths in the Australian States and compare them with those in New Zealand (Table II).

We may with sufficient accuracy for the purpose give death rates per million of population for the different States, using as divisors the number of years in the period multiplied by the population at the middle of the period (Table III).

It is evident that the rates in New Zealand are more favourable than in Australia, and that some of the Australian States such as Victoria have figures comparable with New Zealand. But some disappointment must be expressed that the New South Wales figures and also the Western Australian remain so high.

Yours, etc.,
H. O. LANCASTER.

School of Public Health and Tropical Medicine,
University Grounds,
Sydney.
May 31, 1956.

TRACHOMA IN ABORIGINES.

SIR: I think that the Commonwealth Health Department should take action to eliminate trachoma amongst aborigines in Australia. The disease must be attacked in its early stages, before involvement of the cornea. For over twenty years I have watched this disease in this State, and I believe its incidence and severity has reached an all-time peak.

Yours, etc.,
F. W. SIMPSON, D.O. (Oxon.).

105 St. George's Terrace,
Perth,
Western Australia.
May 26, 1956.

INTERNATIONAL TRENDS IN MEDICINE.

SIR: In your editorial of Saturday, May 19, 1956, entitled "International Trends in Medicine" you advocated an exchange of students between countries as a means of promoting better understanding between them and referred to a communication received by the Federal Council of the British Medical Association from the Fairfield Park Hospital, Cleveland, Ohio, seeking Australian applicants for its internships. In a footnote, reference is made to an advertisement by the Ellis Hospital, Schenectady, New York, with a similar purpose. Your editorial also states, "if one hospital in the United States is far-seeing enough to make such a proposal, surely there are other hospitals in the United States and Great Britain who might be prevailed upon to make the same kind of proposal". About the same time as your editorial appeared, the British Medical Association circular issued in New South Wales set out at some length

TABLE II.

Year.	Deaths from Diphtheria by State.						Australia.	New Zealand.
	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.		
1939	192	42	39	30	27	14	344	24
1940	74	26	24	21	23	18	186	15
1941	121	69	29	41	20	25	305	17
1942	79	47	20	42	41	11	240	24
1943	99	48	50	27	38	15	277	32
1944	69	34	26	18	24	10	181	30
1945	84	39	17	14	20	9	183	42
1946	57	17	20	8	11	6	119	49
1947	49	13	13	5	8	0	88	20
1948[1]	51	10	5	5	7	1	80	3
1949	36	17	18	1	4	0	76	5
1950	25	11	8	1	7	1	53	4
1951	21	7	12	4	11	0	55	3
1952	14	10	7	0	2	0	33	2
1953	33	3	12	1	1	1	51	3

[1] One death in the Northern Territory.

TABLE III.

Years.	Deaths per Million *per Annum* from Diphtheria.							
	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Australia.	New Zealand.
1939 to 1946	34	21	27	41	53	56	32	19
1947 to 1953	10	5	9	4	10	2	8	3
1939 to 1953	23	13	18	23	33	29	20	10

a request for interns from the New England Hospital, Massachusetts, United States of America.

For the past ten years the New South Wales Post-Graduate Committee in Medicine and other post-graduate committees of Australia have interested themselves in this matter, and the Post-Graduate Committee in New South Wales alone arranges, on an average, for about 130 graduates each year to proceed abroad, the majority of whom, at one time or another, serve in hospitals in either the United Kingdom or the United States. Sending graduates abroad for hospital appointments is one thing, exchange is another. So far as Australia is concerned, there are no exchanges. The traffic is one way. Overseas house officers have no interest in Australian hospital appointments, as appointments at the grades that might interest them do not offer the same facilities or responsibilities as the corresponding appointments in their own countries. Apart from this, the few appointments of the type available in Australia are unable to satisfy even the local demand, with the result that large numbers of our own graduates are forced to proceed overseas.

The majority of Australian graduates desiring training overseas proceed to the United Kingdom. Only a few go to the United States. Training in hospitals there is not very popular with Australian graduates, although hospital appointments are not difficult to obtain, as the majority of hospitals in the United States are desperately short of intern and resident staff. Australian graduates who have in the past accepted intern positions in the United States have mostly been very disappointed.

The reason for this unpopularity of the American appointments is that internships in the United States are of a lower grade than our corresponding Australian appointments and offer experience which has more in common with the work of an Australian sixth year medical student than of our first year resident medical officer. This is because the American system of undergraduate medical education corresponds to a five-year course by our reckoning.

In the hospital system of the United States, most of the practical work in the hospitals is done by the residents and assistant residents, who correspond to our registrars. These appointments are of much greater interest to our graduates, but it is usually only after our graduates have served twelve months in a lower grade internship that they can hope to obtain these appointments.

Another factor of importance in regard to the American appointments is that Australian graduates cannot obtain dollars from Australia for their living expenses. This limits them to appointments which provide not only full board and residence, but also sufficient stipend above this to cover their ordinary living expenses. The Post-Graduate Committee in New South Wales, after considerable inquiry, particularly from those who had obtained these appointments, came to the conclusion that 100 dollars a month, in addition to full board and residence, was the barest minimum required for this purpose. The committee accordingly advises any post-graduate proceeding to the United States against accepting any appointment in a hospital there which does not conform with this amongst other requirements. Married men who wish to be accompanied by their wives can usually only take them with them if the wives are able to support themselves by obtaining some kind of a job.

An unusual feature of internships and residentships in the United States is that there is no uniform salary as in the United Kingdom and Australia. The best and most popular hospitals pay little, if any, stipend to their interns, whilst the less attractive hospitals, most of which are not affiliated with any university or teaching institution, are forced by the great shortage of applicants to offer higher stipends. Exceptions to this are the large county and city hospitals, such as the Boston City Hospital and District of Columbia General Hospital, Washington, D.C., which are first-class institutions with good university affiliations which usually pay full maintenance and a stipend of 100 dollars a month. On the other hand, at these hospitals, the task of the intern is even more menial than at most other institutions, as all the worthwhile work which would interest Australian graduates is done by the residents (registrars). If, however, assistant resident or similar posts can be obtained, appointments at these hospitals are particularly suitable for specialist training. Those seeking training suitable for general practice are likely to obtain better all-round experience in some of the smaller outlying hospitals where there is less emphasis on the resident (registrar).

Of the three United States hospitals referred to in the first paragraph of this letter, only one would be considered for recommendation by the New South Wales Post-Graduate Committee. The particulars of the hospitals are as follows:

Hospital.	Number of Beds.	Admissions.	Number of House Staff.	Full Maintenance.	Monthly Stipend. (Dollars.)
Ellis Hospital, Shenectady, N.Y.	358	13,124	10	Yes.	125
Fairview Park Hospital, Cleveland, Ohio	150	7,688	6	Yes.	100
New England Hospital, Boston, Massachusetts	150	3,943	3	Yes.	50

This matter is far from simple, and any Australian graduate desiring hospital appointments overseas or considering applying for them would do well to seek the advice of the post-graduate committee of his particular State before doing so.

Yours, etc.,

V. M. COPPLESON,
Chairman and Honorary Director.

Post-Graduate Committee in Medicine in the University of Sydney,
131 Macquarie Street,
Sydney.
May 25, 1956.

MEDICAL STUDENTS AND COUNTRY GENERAL PRACTICE.

SIR: Last year the Undergraduate Committee of the College of General Practitioners sent two students to Glen Innes, to gain some insight into general practice in the country and the working of a smaller country hospital. These students were so pleased that they re-booked for the May vacation. The local doctors attached to the hospital and the board were so pleased with the arrangement that they gladly concurred.

As the May vacation approached inquiries came in from the two senior years as to the possibility of their being accommodated in other towns. Quick contact was made with college members in country centres which had resident accommodation but no residents. Finally nearly 30 students were sent off to these centres, as many as four going to some of the towns. From reports received the move has been an all-round success. The committee feels that a new institution has been born. It is felt that this exodus to the country will continue indefinitely at least once or twice a year. It should increase in scope and size as the years pass.

Some of the teaching hospitals in Sydney put their students into residence to gain hospital awareness and nursing practice experience. This is very excellent, of course, but does not give any idea of what goes on in an outside community, or what constitutes the daily life of a general practitioner when he leaves the shelter of a specialist hospital.

These boys who are going away will be introduced to the compact working of a smaller hospital and will gain a first-hand knowledge of the pathological and radiological facilities available. They will see expert nursing, which in the absence of the facilities of larger institutions calls for thoughtful improvisation. Perhaps even more important, they will be in close clinical contact for hours daily with cases which are just as interesting and instructive as those in the city. They will gain much by coordinating their newest theories with the keen experience of the country doctors. In addition many of the latter have promised to take them into their general practice and show them what it constitutes. It is realized that this is only a small addition to their training in city hospitals. The finest of clinical teachers are limited, however, by time, numbers, and a heavy curriculum.

The new scheme has a further purpose. We are hoping that awareness of the possibility of country practice gained by close scrutiny will induce more future graduates to undertake it. Many bright young men feel that some sort of specialization is the only future. If they can see opportunities of using some specialized course as a centrepiece of their general practice in some community which they

have seen, whilst participating in the college's scheme, there will be a great gain all round.

There are too many frustrated young men with special degrees and no hospital appointment. The College of General Practitioners has an excellent Post-Graduate Committee working in cooperation with the Post-Graduate Committee in Medicine in the University of Sydney and F.O.C.L.A. It has also a very excellent research body which collects information from all over the State on any given subject and presents the collected evidence to an advisory panel.

In July the first issue of the college's own magazine will start to deal with its members' own special problems, needs and possibilities, and we can offer them help and advice and contact in a measure not attempted before. In fact we feel many rather dubious people must be surprised that we have such full activity in what is obviously our own sphere.

We would be glad to hear from any country centre throughout the State, however remote, in which the local hospital has accommodation but no resident, which would like the services of a senior student, under supervision, during vacation. Our thanks to country practitioners and hospital boards throughout the State, who gave us such willing aid in this initial step. We also are delighted with the cooperation of the Student Medical Society whose help we acknowledge.

Yours, etc.,

T. E. HOLCOMBE,
Chairman, Undergraduate Teaching Committee.

College of General Practitioners,
131 Macquarie Street,
Sydney.
Undated.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

THE Melbourne Medical Post-Graduate Committee, 394 Albert Street, East Melbourne, C.2 (telephone FB 2547), announces the following courses *et cetera*.

PROGRAMME FOR JULY, 1956.

Course in Psychiatry.

The Australasian Association of Psychiatrists will conduct a course of lectures at 8.15 p.m. on Tuesdays and Thursdays from July 10 till August 16. Each lecture will be followed by full discussion, and the course will be suitable as study for candidates for the diploma in psychological medicine and those interested in psychiatry. The time-table, which has already been published, in this journal, is available from the Melbourne Medical Post-Graduate Committee. The fee for the course is £10 10s., or £1 1s. per single lecture. Enrolments should be made through the Post-Graduate Committee on their special form, and will be received until June 25. Concurrently with this course, the Association will arrange seminars in psychotherapy and psychoanalysis, as well as attendance at the psychiatric clinics of the teaching hospitals, Royal Park Receiving House and other institutions and clinics of the Mental Hygiene Department.

Course in Special Pathology for D.D.R. and M.C.R.A.

A course in special pathology for the diploma in diagnostic radiology and membership of the College of Radiologists of Australasia will commence at 4.30 p.m. on Tuesday, July 3, and continue weekly till August 7. The fee for this course is £5 5s., but those already enrolled for the basic pathology need pay no extra fee. Enrolments should be made with the committee by June 25.

Refresher Course at Terang.

A refresher course will be held at Terang on July 21. The programme is as follows: "Management of Burns", Dr. J. C. Stewart and Dr. I. H. Cuming; "Principles of Tissue Conservation and Plastic Repair", Dr. A. R. Wakefield. The local secretary for this course is Dr. W. R. Angus, 214 Koroit Street, Warrnambool.

LECTURES IN AUGUST AND SEPTEMBER, 1956.

There will be a scientific session of the Royal Women's Hospital centenary celebration from August 22 to 28, with Professor Andrew Claye, of Leeds, as guest lecturer.

From August 27 to September 6 Dr. J. H. Sheldon, M.D., F.R.C.P., of Wolverhampton, England, will be in Melbourne. He will visit teaching hospitals and give the following lectures at the British Medical Association Hall at 8.15 p.m. on the dates set out below: August 29, "The Clinical Problems of Old Age"; August 31, "Clinical Problems of Appetite"; September 3, "Obesity, with Particular Reference to Maternal Obesity"; September 6, "Collagen Diseases".

From September 3 to 15 a refresher course in gynæcology and obstetrics for general practitioners will be held at the Royal Women's Hospital.

From September 17 to 21 a refresher course in medicine and surgery for general practitioners will be held.

It is possible that an overseas surgeon may also be here about August, and the committee expects to have a visit from Professor L. J. Witts, of Oxford, from October 7 to 19.

RECORDED LECTURES.

The following have now been added to the committee's library of recorded lectures for microgroove equipment and are available on request: Professor F. R. Winton, M.D., D.Sc., of London: "The Pharmacology of the Kidney", delivered on May 3, 1956, in the British Medical Association Hall (with sheet of illustrations). Professor David Whitteridge, F.R.S., B.Sc., D.M., of Edinburgh: (i) "Recent Advances in Knowledge of Afferent Nerve Fibres from Heart and Lungs", delivered on May 11, 1956; (ii) "Physiological Disturbances in Paraplegia", delivered on May 14, 1956; both these lectures were delivered in the Anatomy Theatre, University of Melbourne, and the records are accompanied by slides three inches square.

CANCER INSTITUTE BOARD.

Tumour clinics will be held at the Cancer Institute, 483 Little Lonsdale Street, Melbourne, at 11.45 a.m. on July 11 and 25 for the purpose of discussing cases of particular interest from the point of view of diagnosis and treatment. Visitors will be welcome to join in the discussion and present cases if they so wish. Contact should be made with Dr. J. P. Madigan or Miss P. Mitchell-Burdon (MU 7831).

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Week-End Course in Endocrinology.

The Post-Graduate Committee in Medicine in the University of Sydney announces that it will hold a week-end course in endocrinology on Saturday and Sunday, July 14 and 15, 1956, in the Scot Skirving Lecture Theatre, Royal Prince Alfred Hospital. The course has been aimed at the advanced medicine candidate and the general practitioner with a special interest in internal medicine. The programme is as follows:

Saturday, July 14: 2 p.m., introduction, Dr. T. M. Greenaway; 2.15 p.m., "Pituitary Insufficiency", Dr. K. S. Harrison; 2.45 p.m., "Treatment of Hyperthyroidism", Dr. F. F. Rundle; 3.15 p.m., "Assessment of Adrenal Function", Dr. P. F. Hall; 4 p.m., panel discussion, "Basic Endocrinology".

Sunday, July 15: 10 a.m., "Parathyroid Hypofunction and Tetany", Dr. L. C. A. Watson; 10.30 a.m., "The Endocrine Factor in Growth", Dr. R. H. Vines; 11.15 a.m., "Addison's Disease", Dr. K. S. Harrison; 11.45 a.m., "Endocrine Disorders of the Ovary", Dr. P. F. Hall; 12.15 p.m., "Hyperparathyroidism", Dr. L. C. A. Watson; 2 p.m., "The Anomalies of Puberty", Dr. R. H. Vines; 2.30 p.m., "Principles of Adrenal Steroid Therapy", Dr. T. M. Greenaway; 3 p.m., "Eye Changes in Hyperthyroidism", Dr. F. F. Rundle; 3.45 p.m., panel discussion, "Endocrine Therapy".

The fee for attendance at the course is £3 3s., and those wishing to attend are requested to make written application, enclosing remittance, to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-4498. Telegraphic address: "Postgrad Sydney."

Part II Course for Diploma in Anæsthesia.

The Part II course for the diploma in anæsthesia is due to begin on July 16, 1956, and will continue until December, with a recess during the Part I course in September-November. Those wishing to enrol are requested to make early application to the Course Secretary, Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-4498. Telegraphic address: "Postgrad Sydney."

Medical Practice.

NATIONAL HEALTH ACT.

THE following notice appeared in the *Commonwealth of Australia Gazette*, Number 29, of June 7, 1956.

NATIONAL HEALTH ACT, 1953-1955.

Part IV: Pensioner Medical Service.

Reprimand of Medical Practitioner.

I, DONALD ALASTAIR CAMERON, the Minister of State for Health, hereby give notice, in pursuance of sub-section (1) of section 134A of the *National Health Act*, 1953-1955, that I have this day reprimanded Keith Reye of Gin Gin, medical practitioner, following investigation and report by the Medical Services Committee of Inquiry for the State of Queensland established under Section 110 of the *National Health Act*, 1953, concerning the conduct of the aforesaid medical practitioner in relation to his provision of medical services for pensioners and their dependants under Part IV of the *Natonal Health Act*, 1953-1955, or under an arrangement made by the Director-General of Health under Section 7 of the *National Health Service Act*, 1948-1949, and the National Health (Medical Services to Pensioners) Regulations.

Dated this 18th day of May, 1956.

DONALD A. CAMERON,
Minister of State for Health.

Honours.

BIRTHDAY HONOURS.

IN the list of Birthday Honours published in our issue of June 9, 1956, the name of Dr. William Alexander Sloss, of Ballarat, was omitted. We regret this omission. Dr. Sloss's name did not appear in any of the newspapers at our disposal. The award was discovered on receipt of the air mail copy of the *British Medical Journal* of June 9, 1956. Dr. Sloss has been created a Member of the Most Excellent Order of the British Empire.

In our recent announcement of honours conferred by Her Majesty on medical practitioners, the name of Dr. Leonard James Pellew was wrongly stated as Leonard James Ternouth Pellew. It is the former who has been created a Commander of the Most Excellent Order of the British Empire. This error is regretted.

Medical Prizes.

AUSTRALIAN SOCIETY OF ANÆSTHETISTS' PRIZE.

THE Australian Society of Anæsthetists is offering an annual prize of £25 for the best original paper submitted by an anæsthetist in Australia holding the grading of senior registrar or under at the time of submission of the paper. It is not necessary that he or she be a member of the Society.

The conditions are as follows: (i) The paper must be original—that is, it should not have been previously read at any meeting or published in any journal. (ii) It is desirable that papers submitted show evidence of personal work; but papers consisting of surveys of the literature are eligible for consideration. The Executive of the Australian Society of Anæsthetists wishes to stress that intending competitors should not be discouraged through fear of their

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JUNE 2, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	2(2)	2(2)	3(1)	..	..	..	..	9
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	1	..	..	..	..	..	1
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	1(1)	1(1)	..	1(1)	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	2(2)	7(6)	..	..	..	..	..	..	9
Diphtheria	5(2)	3(3)	..	1(1)	6(5)	..	1	..	16
Dysentery (Bacillary)	..	2(2)	5(2)	..	1(1)	..	..	..	8
Encephalitis	1	2	..	..	..	..	..	..	3
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	63(32)	41(25)	..	7(4)	1(1)	4	1	..	117
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	3	..	10(1)	..	..	..	..	..	13
Malaria	..	..	2(2)	..	..	..	..	..	2
Meningococcal Infection	2(1)	2(1)	1	..	..	..	..	..	5
Ophthalmia	..	..	..	..	..	..	1	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	9(5)	10(9)	2(1)	2(1)	7	..	..	..	30
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	10(3)	..	7	1(1)	..	..	..	18
Salmonella Infection	..	..	..	3(3)	3(2)	..	..	..	6
Scarlet Fever	15(11)	13(11)	..	8(6)	..	..	..	1	37
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	1(1)	..	..	..	..	..	1
Trachoma	..	..	..	..	5(4)	..	..	..	5
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	11(8)	24(13)	14(5)	3(3)	8(7)	2(2)	2	..	64
Typhoid Fever	1(1)	..	..	..	..	..	..	..	1
Typhus (Flea-, Mite- and Tick-borne)	..	..	2(2)	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

efforts being elementary. If, however, there is no paper of sufficient merit, the prize may be withheld and the amount added on to the award for the following year. (iii) The subject of the paper submitted is left to the choice of each author, but the chosen subject must be connected with anæsthesia. (iv) The winner of the prize will be required to read his paper at the annual general meeting of the Australian Society of Anæsthetists.

Papers for the 1956 prize should reach the Honorary Secretary, Dr. Patricia Wilson, c.o. Department of Anæsthesia, The Royal Melbourne Hospital, Victoria, not later than December 1, 1956.

Notice.

SPECIAL GROUP ON AVIATION MEDICINE (BRITISH MEDICAL ASSOCIATION).

THE Special Group on Aviation Medicine (British Medical Association) will hold a scientific meeting on July 5, 1956, at 8 p.m., in the William H. Crago Council Chamber, British Medical Association House, 135 Macquarie Street, Sydney. The programme will include a talk by Surgeon Commander R. M. Coplans, R.A.N., entitled "Some Recent Advances in Aviation Medicine", which will cover his recent tour of Farnborough and other service and civil aviation centres in the United Kingdom. All interested members of the British Medical Association are invited to attend the meeting.

INTERNATIONAL MEDICO-SURGICAL MEETINGS.

WE have been asked to announce that the third International Medical and Health Exhibition and the third International Medical and Scientific Film Festival will be held under the auspices of *Minerva Medica* at Turin, Italy, from June 1 to 9, 1957. The 1957 meetings will be dedicated to the work of Angelo Mosso (1846 to 1910), who made many contributions to the knowledge of physiology, introduced an ergograph for the study of voluntary contraction of muscle, carried out important studies in fatigue and on respiration at high altitudes, and invented a sphygmomanometer. Inquiries may be made from the General Secretariat, c.o. *Minerva Medica, Corso Bramante* 83-85, Turin, Italy.

Australian Medical Board Proceedings.

QUEENSLAND.

THE following has been granted limited registration as a medical practitioner, pursuant to Section 20 (3) of *The Medical Acts*, 1939 to 1955, of Queensland: Carroll, Alan, M.B., B.S., 1954 (Univ. Melbourne).

The following have been registered, pursuant to the provisions of Section 19 (1) (*a*) and (*d*) of *The Medical Acts*, 1939 to 1955, of Queensland, as duly qualified medical practitioners: Elliott, Margaret Helen, M.B., B.Ch., B.A.O., 1922 (Q.U. Belfast), D.P.H. (1923) (Q.U. Belfast); Jamieson, Kenneth Grant, M.B., B.S., 1948 (Univ. Melbourne).

The following has been registered, pursuant to the provisions of Section 19 (1) (*a*) and (*e*) of *The Medical Acts*, 1939 to 1955, of Queensland, as a duly qualified medical practitioner: Crotty, John Martin, M.B., B.S., 1950 (Univ. Melbourne).

The following has been registered, pursuant to the provisions of Section 19 (1) (*a*) and (*c*) of *The Medical Acts*, 1939 to 1955, of Queensland, as a duly qualified medical practitioner: Cecil, Kevin Howard, M.B., B.S., 1955 (Univ. Melbourne).

The following additional qualification has been registered: Maguire, William Brian, F.R.C.S. (England), 1955.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Andrews, Bruce Allan, M.B., B.S., 1955 (Univ. Sydney), Broken Hill and District Hospital, Broken Hill, New South Wales.

McClure, Eunice Mary, M.B., B.S., 1955 (Univ. Sydney), Broken Hill and District Hospital, Broken Hill, New South Wales.

Smith, Ronald James, M.B., B.S., 1955 (Univ. Sydney), Lake Street, Lake Cargelligo, New South Wales.

Havas, Laszlo, registered in accordance with the provisions of Section 17 (1) (*c*) of the *Medical Practitioners Act*, 1938-1955, 42 Hastings Parade, North Bondi, New South Wales.

Deaths.

THE following deaths have been announced:

O'CONNOR.—Joseph Lionel O'Connor, on June 4, 1956, at Melbourne.

APPS.—Ray Clifton Apps, on June 8, 1956, at Berry, New South Wales.

SWAIN.—Alex Benjamin Swain, on June 9, 1956, at Melbourne.

Diary for the Month.

JUNE 26.—New South Wales Branch, B.M.A.: Ethics Committee.
JUNE 27.—Victorian Branch, B.M.A.: Branch Council.
JUNE 28.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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